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(FILE 'HOME' ENTERED AT 11:58:17 ON 01 JUN 2010)
    FILE 'CAPLUS' ENTERED AT 11:58:25 ON 01 JUN 2010
L1
              2 S WO 2004087731/PN
                SELECT RN L1 1-
    FILE 'REGISTRY' ENTERED AT 11:59:17 ON 01 JUN 2010
L2
             17 S E1-17
L3
              6 S 5-6-6-6/SZ AND L2
L4
             11 S L2 NOT L3
L5
          17324 S 4432.3.25/RID
           902 S CARBOTHIO? AND L5
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          4352 S L7 SSS FUL
L10
               STRUCTURE UPLOADED
           1945 S L10 SUB=L9 FUL
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     FILE 'CAPLUS' ENTERED AT 12:11:02 ON 01 JUN 2010
L12
           2318 S L11
     FILE 'REGISTRY' ENTERED AT 12:13:55 ON 01 JUN 2010
     FILE 'CAPLUS' ENTERED AT 12:14:28 ON 01 JUN 2010
                S C24 H30 F2 O5 S/MF
    FILE 'REGISTRY' ENTERED AT 12:14:37 ON 01 JUN 2010
            21 S C24 H30 F2 O5 S/MF
L13
    FILE 'CAPLUS' ENTERED AT 12:14:38 ON 01 JUN 2010
L14
            45 S L13
L15
             35 S L3 AND L14
    FILE 'REGISTRY' ENTERED AT 12:14:59 ON 01 JUN 2010
L16
             21 S C24 H30 F2 O5 S/MF
L17
              1 S L16 AND L3
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28 S L17 L19

25 S L18 NOT (2010/SO OR 2009/SO OR 2008/SO OR 2007/SO OR 2006/SO

FILE 'CAPLUS' ENTERED AT 12:15:24 ON 01 JUN 2010

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10/552,118

L19 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:1370146 CAPLUS

DOCUMENT NUMBER: 151:508769
TITLE: Process for

TITLE: Process for synthesis of

androstane- 17β -carbothioic acid and related

derivatives thereof

INVENTOR(S): Hsu, Nai-Hsuan; Pang, Chu-Yi; Wu, Chien-Jen; Huang,

Chi-Jen; Hsu, Chia-Jung; Lee, Peimin

PATENT ASSIGNEE(S): Corum Inc., Taiwan

SOURCE: U.S. Pat. Appl. Publ., 6pp.

Ι

CODEN: USXXCO
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20090275767	A1	20091105	US 2008-112229	20080430
PRIORITY APPLN. INFO.:			US 2008-112229	20080430
ASSIGNMENT HISTORY FOR	US PATEN	T AVAILABLE	IN LSUS DISPLAY FORMAT	
OTHER SOURCE(S):	MARPAT	151:508769		

R CO OR17?

- AB A process was disclosed for synthesis of androstane-17B-carbothioic acid derivs., such as I [R = SH, alkylthio, haloalkylthio, etc.; R17a = acyl], without addition of hydrogen sulfide. The process comprised a one-pot reaction of a corresponding androstane-17B-carboxylic acid, such as I [R = OH, R17a = H] with an carbothioic acid, such as R17aSH, using a coupling reagent. Thus, carbothioic acid derivative I [R = SH, R17a = CCCRZMe] was prepared by reacting carboxylic acid I [R = OH, R17a = H] with propanethioic acid using N,N'-carbonyldimidazole in THF at 5° for 18 h under nitrogen.
- IT 80474-45-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

- (process for preparation of androstane-17 β -carbothioic acid derivs.) RN 80474-45-9 CAPLUS
- CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6 α ,11 β ,16 α ,17 α)- (CA INDEX NAME)

L19 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:237775 CAPLUS

DOCUMENT NUMBER: 148:355999

TITLE: Method for preparing fluticasone propionate

INVENTOR(S): Shen, Yuliang, Liu, Xirong, Xie, Laibin; He, Huixian
PATENT ASSIGNEE(S): Hunan Steroid Chemicals Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenging Gongkai Shuomingshu, Ilpo.

CODEN: CNXXEV
DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO.	KIND	DATE	API	PLICATION NO.	DATE
CN 101125875	A	20080220	CN	2007-10044880	20070815
CN 100549022	C	20091014			
PRIORITY APPLN. INFO.:			CN	2007-10044880	20070815

OTHER SOURCE(S): CASREACT 148:355999

GI

AB Fluticasone propionate is prepared by (1) allowing to react compound 1(6α,9α-difluoro-11β-hydroxy-16α-methyl-17α-

propionyloxy-3-one-androst-1,4-diene-17 β -thiocarboxylate) with XCH2 α r (X = Cl, Br, iodo) at a molar ration of 1-5:1 in solvent in the presence of alkali at 0-150°C for 0.2-5 h to obtain halide I; (2) then reacting with ammonium tetraalkyl fluoride or M+ Γ = in the presence of ion solution and solvent at 20-100°C for 0.1-24 h to obtain the product with formula 3, wherein M+ Γ is fluoride of alkaline metal ion, alkaline earth metal ion or transition metal ion; alkali is hydroxide, phosphate or

carbonate of alkaline metal or alkaline earth metal, or organic base. Ion solution is

[Bmim][X], wherein [Bmim] is 1-butyl-3-methylimidazole; [X] is BF4, PF6, SbF6, OTf or NTF2. Solvent used in step (1) is DMSO, N,N-DMF, acetone, methanol, ethanol, acetonitrile, dichloromethane, petroleum ether, toluene and/or xylene; solvent used in step (2) is DMSO, N,N-DMF, acetone, ethanol, acetonitrile, 1,4-dioxane, tert-butanol, dichloromethane, petroleum ether, toluene and/or xylene. Tetraalkylammonium fluoride is Cl-C2O tetraammonium fluoride with or without crystal water. The molar ratio of tetraalkylammonium fluoride to I, M+F- to I and ion solution to I is 1-5:1, 1-6:1 and 0.1-6:1 resp. The method has advantages of simple operation process, high yield, low cost, convenience for post treatment

and promising industrial prospect.

IT 80474-45-9

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of fluticasone propionate)

RN 80474-45-9 CAPLUS

L19 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:998622 CAPLUS DOCUMENT NUMBER: 147:344254

TITLE: Preparation of novel

11β-hydroxyandrost-4-en-3-ones for therapeutic use as anti-inflammatory agents

Patel, Jiten Ranchhodbhai; Patel, Gopalkumar INVENTOR(S): Chimanlal; Sheth, Gaurav Sanjivkumar; Shah, Samir Rameshchandra; Mandhane, Sanjay Nandlal; Chitturi,

Trinadha Rao; Thennati, Rajamannar

PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Limited, India

SOURCE: PCT Int. Appl., 128pp.

CODEN: PIXXD2 DOCUMENT TYPE: Patent

LANGUAGE . English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

	TENT				KIN		DATE					TION				ATE	
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												SE,					
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		GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ	, TZ	UG,	ZM,	ZW,	AM,	AZ,	BY,
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	2637											-2637					
EP	2004	667			A2		2008	1224		ΕP	2007	-7365	11		2	0070	129
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	2009						2009					-5519					
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	2009						2009					-1802					
	1013											-8000					
	2008				A		2008	1014				-7201				0080	
PRIORIT:	Y APP	LN.	INFO	. :								-MU13					
										WO	2007	-IN39			W 2	0070	129

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): MARPAT 147:344254

GI

AB 11β -Hydroxyandrost-4-en-3-one derivs., such as I [1,2-bond = single or double; R6 = H, F; R9 = Cl, F; R16 = H, α -, β -Me; R17 = alkyl, alkoxy, aryl, heteroaryl; R20 = alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocyclyl, etc.; Z = O, S, S-Ol, were prepared as glucocorticoid receptor ligands for use in anti-inflammatory pharmaceutical compns. Thus, 11β -hydroxyandrost-4-en-3-one derivative II was prepared via an esterification reaction of acid I (R6 = R9 = F, R16 = α -Me, R17 = CH2Me, R20 = H, Z = O) with PhCCH2Br. The prepared 11β -hydroxyandrost-4-en-3-ones were screened for glucocorticoid receptor binding activity using radioligand binding assays and for anti-inflammatory activity using a cotton pellet granuloma screen in rats.

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of 11β -hydroxyandrost-4-en-3-ones for therapeutic use as anti-inflammatory agents)

RN 80474-45-9 CAPLUS CN Androsta-1,4-diene

Androsta-1, 4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, $(6\alpha,11B,16\alpha,17\alpha)$ - (CA INDEX NAME)

L19 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

2007:789323 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 147:257929

TITLE: Method for synthesis of Fluticasone propionate

INVENTOR(S): Qin, Guoru

PATENT ASSIGNEE(S): Gaoyou Zhaokang Pharmaceutical Co., Ltd., Peop. Rep.

China

SOURCE: Faming Zhuanli Shenging Gongkai Shuomingshu, 18pp.

CODEN: CNXXEV DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO.	KIND	DATE	AP.	PLICATION NO.	DATE
CN 100999541	A	20070718	CN	2006-10161627	20061219
CN 100497367	С	20090610			
PRIORITY APPLN. INFO.:			CN	2006-10161627	20061219
OTHER SOURCE(S):	CASRE	ACT 147:2579:	29		

The title compound was synthesized from Flumethasone oxidation with sodium

periodate or periodic acid to obtain

6α.9α-difluoro-11β,17α-dihydroxyl-16α-methyl-

3-oxy-androstane-1, $4-diene-17\beta-carboxylic acid$; thiolation with

N, N-dimethylthioaminoformyl chloride in the presence of

diisopropylethylamine; and potassium iodide to give

6α,9α-difluoro-11β-hydroxyl-16α-methyl-3-oxy-

androstane-1,4-diene-17β-thiocarboxylic acid; esterification with

propanoyl chloride; and sulfur alkylation with bromofluoromethane in the presence of potassium carbonate as catalyst. This invention has the advantages of a short reaction process, high yield, low cost, and high

product purity. 80474-45-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent) (synthesis of Fluticasone propionate from Flumethasone)

RN 80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hvdroxv-16-methv1-3-oxo-17-(1-oxopropoxv)-,

(6α, 11B, 16α, 17α) - (CA INDEX NAME)

L19 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:113502 CAPLUS

DOCUMENT NUMBER: 146:184636

TITLE: Method for preparation of Fluticasone propionate

INVENTOR(S): Chu, Dingjun; Zhang, Defa

PATENT ASSIGNEE(S): Shanghai Aurisco International Trading Co., Ltd.,

Peop. Rep. China

SOURCE: PCT Int. Appl., 14pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

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	PATENT														D.	ATE	
	WO 2007														2	0050	829
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		SL,	SM.	SY,	TJ.	TM.	TN.	TR.	TT,	TZ.	UA.	UG,	US.	UZ,	VC.	VN.	YU.
		ZA,	ZM,	ZW													
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	CN 1903 CN 1005 EP 1911	871			A		2007	0131		CN 2	005-	1002	8147		2	0050	726
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	EP 1911	741			A1		2008	0416		EP 2	005-	7818	41		2	0050	829
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	US 2008	0125	407		A1		2008	0529		US 2	008-	2051	9		2	0080	126
	IN 2008	DN01	479		A		2008	0404		IN 2	008-	DN 14	79		2	0080	220
PRIO	US 2008 IN 2008 RITY APP	LN.	INFO	. :						CN 2	005-	1002	8147		A 2	0050	726
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6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-,

 $(6\alpha,11\beta,16\alpha,17\alpha)- \quad \text{(CA INDEX NAME)}$ Absolute stereochemistry. Rotation (-).

2

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2006:381179 CAPLUS

DOCUMENT NUMBER: 144:412741

TITLE: Process for preparation of fluticasone analogs via

esterification of a carbothioic acid

INVENTOR(S): Sobral, Luis; Martin, Dionisio; Heggie, William;

Leitaeo, Emilia

PATENT ASSIGNEE(S): Hovione Inter Ltd., Switz.; Turner, Craig Robert

SOURCE: PCT Int. Appl., 18 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

E	PAT	ENT I	. OV			KIN		DATE				PLICAT				D.	ATE	
To To	٧O	2006	0430	15		A1						2004-				2	0041	202
		W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BE	BG,	BR,	BW,	BY,	BZ,	CA,	CH,
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			GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS	JP,	KE,	KG,	KP,	KR,	KZ,	LC,
			LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG	G, MK,	MN,	MW,	MX,	MZ,	NA,	NI,
			NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU	J, SC,	SD,	SE,	SG,	SK,	SL,	SY,
			TJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US	s, UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW
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			IS,	IT,	LT,	LU,	MC,	NL,	PL,	PT,	RO	, SE,	SI,	SK,	TR,	BF,	ВJ,	CF,
			CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MF	R, NE,	SN,	TD,	TG,	BW,	GH,	GM,
			KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	T2	, UG,	ZM,	ZW,	AM,	ΑZ,	BY,	KG,
			KZ,	MD,	RU,	TJ,	TM											
												2004-						
(CA	2584	052			A1		2006	0427		CA	2004-	2584	052		2	0041	202
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			IS,	IT,	LI,	LT,	LU,	MC,	NL,	PL,	P1	r, RO,	SE,	SI,	SK,	TR		
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F	RU	2351	605			C2						2007-						
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N	10	2007	0019	96		A		2007	0706		NO	2007-	1996			2	0070	419
1	IN	2007	DN03	197		A		2007	0831		IN	2007-	DN31	97		2	0070	427
Ţ	JS	2007	0287	846		A1		2007	1213		US	2007-	5774	62		2	0070	731
PRIORI	ΙTΣ	APP:	LN.	INFO	. :						PΤ	2004-	1032	02		A 2	0041	019
											WO	2004-	GB50	52		W 2	0041	202

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 144:412741
GI

10/552,118

AB A process for preparing esters, such as I (R = CO(CH2)n, COCHMe2, n = 1, 2), was disclosed and comprised esterification of the C-17 hydroxyl group of 6α, 9α-difluoro-11β, 17α-dihydroxy-16α-methyl-3-oxoandrosta-1, 4-diene-17β-carbothioic acid I (R = H) with a slight excess of a corresponding acyl chloride, RCOCl, in an inert solvent in the presence of a tertiary amine.
II
80.474-45-9P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (USes)

(process for preparation of pharmaceutically useful fluticasone analogs via esterification of a corresponding carbothioic acid) 80474-45-9 CAPLUS

RN 80474-45-9 CAPLUS CN Androsta-1,4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6α,11β,16α,17α)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2006:74597 CAPLUS

DOCUMENT NUMBER: 144:156707

TITLE: Novel crystalline forms of 6α , 9α -difluoro- 11β -hydroxy- 16α -

methyl-3-oxo-17a-propionyloxy-androsta-1,4-diene 17 β -carboxylic acid and processes for preparation

INVENTOR(S): Adin, Itai; Iustain, Carmen; Futerman, Yuri

PATENT ASSIGNEE(S): Chemagis Ltd., Israel

SOURCE: U.S. Pat. Appl. Publ., 46 pp.

CODEN: USXXCO
DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

P	'A'	ENT	NO.			KIN	D	DATE			APPL	ICAT	ION	NO.		D.	ATE	
Ċ	A	2006 2575 2006	376			A1		2006 2006 2006	0202		CA 2	005- 005- 005-	2575	376		2		726
W	Ю	2006	0111	48		A3		2009	0108									
		W:	CN,	co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	BG, EC, JP,	EE,	EG,	ES,	FI,	GB,	GD,
			LC, NG,	LK, NI,	LR, NO,	LS, NZ,	LT, OM,	LU, PG,	LV, PH,	MA, PL,	MD, PT,	MG, RO,	MK, RU,	MN, SC,	MW, SD,	MX, SE,	MZ, SG,	NA, SK,
		211	ZA,	ZM,	ZW	·		·				UA,			·			
		KW:	IS,	IT,	LT,	LU,	LV,	MC,	NL,	PL,	PT,	ES, RO, MR,	SE,	SI,	SK,	TR,	BF,	ВJ,
			GM,	KE, KZ,	LS, MD,	MW, RU,	MZ, TJ,	NA, TM,	SD, AP,	SL, EA,	SZ, EP,	TZ, OA	UG,	ZM,	ZW,			
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												004-					0040	
											WO 2	005-	IL80:	2	1	й 2	0050	726

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT AB Novel crystalline forms II, III, IV, V, VI, VII and VIII of

6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-propionyloxyandrosta-1,4-diene-17β-carboxylic acid, a chemical

intermediate useful in the preparation of fluticasone propionate, and novel methods of making these forms, substantially free of water, are disclosed. 80474-45-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(crystalline forms of 6α , 9α -difluoro- 11β -hydroxy- 16α -methyl-3-oxo- 17α -propionyloxy-androsta-1, 4-diene

 17β -carboxylic acid for prpg. fluticasone propionate)

RN 80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, $(6\alpha,11\beta,16\alpha,17\alpha)$ - (CA INDEX NAME)

L19 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2006:36999 CAPLUS

DOCUMENT NUMBER: 144:108501

TITLE: Synthesis and powder preparation of fluticasone

propionate

INVENTOR(S): Kaspi, Joseph; Arad, Oded; Brand, Michael; Shookrun,

Moty; Malka, Simona; Alnabari, Mohammed; Hazan,

Shalom; Malesevic, Vlado

PATENT ASSIGNEE(S): Israel

SOURCE: U.S. Pat. Appl. Publ., 27 pp.

CODEN: USXXCO DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060009435	A1	20060112	US 2005-159241	20050623
PRIORITY APPLN. INFO.:			US 2004-581702P P	20040623
			US 2004-623877P P	20041102

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): CASREACT 144:108501

AB Fluticasone propionate is prepared from the thiocarboxylic acid precursor and a halofluoromethane in the presence of water and a base in an organic solvent. The prepared fluticasone propionate is spray dried to form a powder that is highly suitable for administration by inhalation. A process of purifying a key intermediate in the synthesis of fluticasone propionate is also disclosed.

80474-45-9

RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis and powder preparation of fluticasone propionate) 80474-45-9 CAPLUS

RN 80474-45-9 CAPLUS CN Androsta-1,4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA INDEX NAME)

10/552,118

L19 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:361853 CAPLUS

DOCUMENT NUMBER: 142:411529

TITLE: A process for preparing androstane 17β-carboxylic

acids and androstane 17B-carbothioic acid

fluoromethyl esters

Vetturini, Emanuela; Farnesi, Sara INVENTOR(S): PATENT ASSIGNEE(S): S.N.I.F.F. Italia S.p.A., Italy

SOURCE: Eur. Pat. Appl., 20 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO.	KI	ND DATE	AP	PLICATION N	NO.	DATE
EP 1526139	F	1 2005	0427 EF	2003-24329	9	20031024
	, BE, CH, DE					
IE	, SI, LT, LV	, FI, RO,	MK, CY, A	L, TR, BG,	CZ, EE, H	U, SK
US 2005009	0675 P	.1 2005	0428 US	2004-9692	41	20041021
PRIORITY APPLN.	INFO.:		EP	2003-24329	9 A	20031024
ASSIGNMENT HIST	ORY FOR US F	ATENT AVA	ILABLE IN	LSUS DISPLA	AY FORMAT	
OTHER SOURCE(S)	: CF	SREACT 14	2:411529;	MARPAT 142	:411529	
GT						

- AB The present invention relates to an oxidation process for preparing androstane 17β -carboxylic acid derivs., such as I [R1, R2 = H, OH; R1R2 = O; X, Y = C1, F; R3 = α -Me, β -Me; R4 = OH, alkanoyloxy; R5 = OH], with a high purity degree by oxidative demolition of the carbon atom 21 of the compound II [R5 = CH2OH] by using hydrogen peroxide in a basic environment in a polar solvent optionally in the presence of water. The invention also discloses a process for preparing fluticasone propionate II [R = CH2F] from androstane-17 β -carbothioic acid derivative II [R = H] and bromofluoromethane.
- 80474-45-9

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of androstane 17B-carboxylic acids and androstane 17β-carbothioic acid fluoromethyl esters)

- RN 80474-45-9 CAPLUS
- CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methy1-3-oxo-17-(1-oxopropoxy)-,

10/552,118

 $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA INDEX NAME)

7

Absolute stereochemistry. Rotation (-).

REFERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:857616 CAPLUS

DOCUMENT NUMBER: 141:332364

TITLE: Process for the preparation of steroidal carbothioic

acid derivatives and intermediates

INVENTOR(S): Loevli, Trond; Nygaard, Anne-mette; Reitstoen, Bjoern;

Fivelstad, Magny PATENT ASSIGNEE(S): Alpharma Aps. Den.

SOURCE: PCT Int. Appl., 40 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

	rent :									APPL								
	2004																	
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,	
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NA,	NI,	
								PT,										
		ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW	
	RW:	BW,	GH,	GM,	KΕ,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	
								TM,										
								ΙE,										
				BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	
		TD,																
EP					A1 20041013													
	R:																PT,	
								MK,										
	2004									AU 2	004-	2263	18		2	0040	402	
	2004																	
	2530																	
EP	1611																	
	R:							FR,										
TD	2000							MK,										HR
	2006																	
					A 20051227 A 20070406													
	2003															0051		
OS IORIT					AI		2007	1122		US 2								
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										WO 2	004-	443 1	2		n 2	0040	713	
										WO Z	004-	DICZ4	~		v: 2	0040	402	

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT CASREACT 141:332364; MARPAT 141:332364 OTHER SOURCE(S):

6α,9α-difluoro-11β-hydroxy-16α-methy1-3-oxo-

AB Steroidal carboxthioc acids were prepared by reacting steroidal carboxylic acids or salts with a coupling agent alone or in conjunction with a coupling enhancer followed by reaction with a nucleophilic agent comprising a sulfur atom. Thus, 6α , 9α -difluoro- 11β -hydroxy- 16α -methyl-3-oxo- 17α -propionyloxyandrosta-1,, 4-diene-

¹⁷β-carboxylic acid, prepared from flumetasone, in DMA was treated with EDC (1-ethyl-3-(3-dimethylaminopropyl)carbodimide) and NHS

⁽N-hydroxysuccinimide) followed by sodium hydrosulfide hydrate and then bromofluoromethane to give 92% S-fluoromethyl

 $17\alpha\text{-propionyloxyandrosta-1,4-diene-17}\beta\text{-carbothioate}$

(fluticasone propionate).

IT 80474-45-9P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for preparation of steroidal carbothioic acid derivs. and intermediates)

RN 80474-45-9 CAPLUS

CN Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6a,11B,16a,17a)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

REFERENCE COUNT:

14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:837305 CAPLUS

DOCUMENT NUMBER: 141:332363

TITLE: Process for the preparation of steroidal

17β-carbothioates

INVENTOR(S): Loevli, Trond; Nygard, Anne Mette; Reitstoen, Bjoern;

Fivelstad, Magny
PATENT ASSIGNEE(S): Alpharma Aps, Den.

SOURCE: Eur. Pat. Appl., 18 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION:

PA:	TENT	NO.			KIN	D	DATE						NO.		D.	ATE		
EP	1466	920			A1		2004	1013							2	0030	404	
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
		IE.	SI.	LT.	LV.	FI.	RO.	MK.	CY.	AL.	TR.	BG.	CZ.	EE.	HU.	SK		
AU	2004	2263	18		A1		2004	1014		AU 2	004-	2263	18		2	0040	402	
AU	2004	2263	18		B2		2008	0605										
CA	2530	680			A1		2004	1014		CA 2	004-	2530	680		2	0040	402	
WO	2004	0877	31		A1		2004	1014		WO 2	004-	DK24	2		2	0040	402	
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		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NA,	ΝI,	
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	
		TJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UΖ,	VC,	VN,	YU,	ZA,	ZM,	zw	
	RW:	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	
		BY,	KG,	KZ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	
		ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	
		SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	
		TD,	TG															
EP	1611	149			A1		2006	0104		EP 2	004-	7253	01		2	0040	402	
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
		IE,	SI,				RO,											HR
	1798				A		2006	0705		CN 2	004-	8001	5412		2	0040	402	
	2006																	
	2005																	
	2005																	
	2007				A1		2007	1122										
ORIT	Y APP	LN.	INFO	.:														
										DK 2	004 -	449			A 2	0040.	319	

WO 2004-DK242 W 20040402

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): MARPAT 141:332363

GI

- AB A novel method was disclosed for the conversion of steroidal 17 β -carboxylic acids I (Z = 0H) to the corresponding carbothioates I [R1 = H, OH, acyloxy; R2 = H, α -OH, α -, β -alkyl; R1R2 = fused 1,3-dioxolane ring of the form -OCRYR8O-; R3 = OH, protected hydroxyl; R4 = H, halogen; R3R4 = bond, -O- (epoxide); R5 = H, halogen; R7, R8 = H, alkyl; Z = SCH2F, SCH2Br, S(CH2)2F] including fluticasone propionate II (R1 = COCH2Me, Z = SCH2F), via novel in situ generated 17 β -carboxy imidazolyl- or succinimidyl esters. Thus, flumetasone II (R1 = OH, Z = CH2OH) was oxidized using periodic acid to form the corresponding acid II (R1 = Z = OH) in 98% yield. The the acid was esterified with MeCH2COCl using NEt3 to give 17 α -propionate II (R1 = OCCCH2Me, Z = OH) in 99% yield, and subsequent treatment of the 17 α -propionate with NHS and FCH2Br gave fluticasone propionate in 75% yield.
- IIT 80474-45-9P
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
 (Preparation)
- (process for the preparation of steroidal 17β -carbothioates) RN 80474-45-9 CAPLUS
- CN Androsta-1, 4-diene-17-carbothioic acid,
 - 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, $(6\alpha,11\beta,16\alpha,17\alpha)$ (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

REFERENCE COUNT:

3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L19 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:515530 CAPLUS

DOCUMENT NUMBER: 141:54528

TITLE: Preparation of 17β -fluorinated-androstane esters from androstane 17β -carbothioate intermediates

INVENTOR(S): Da Col, Marco; Cainelli, Gianfranco; Umani Ronchi,

Achille; Sandri, Sergio; Contento, Michele; Fortunato, Giuseppe

PATENT ASSIGNEE(S): Farmabios S.R.L., Italy; Boriani, Maria Adele

SOURCE: PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PAT	TENT :	NO.			KIN	D	DATE			APPL	ICAT				D	ATE		
WO	2004	0529	 12		A1	-	2004	0624		WO 2					2	0031	208	
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,	
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	GE,	
		GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KΡ,	KR,	ΚZ,	LC,	LK,	
		LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NI,	NO,	NZ,	
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		BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	
		ES,	FI,	FR,	GB,	GR,	HU,	IE,	ΙT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	
		TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG
CA	2510	609			A1		2004	0624		CA 2	003-	2510	609		2	0031	208	
AU	2003	2938	03		A1		2004	0630		AU 2	003-	2938	03		2	0031	208	
EP	1575	983			A1		2005	0921		EP 2	003-	7891	76		2	0031	208	
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
		ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	SK		
JP	2006	5155	81		T		2006	0601		JP 2	004-	5580	31		2	0031	208	
MX	2005	0061	06		A		2005	1214		MX 2	005-	6106			2	0050	608	
US	2006	0116	359		A1		2006	0601		US 2	005-	5380	83		2	0050	608	
IN	2005	CN01	524		A		2007	0622		IN 2	005-	CN15	24		2	0050	705	
RITY	Y APP	LN.	INFO	. :						IT 2	002-	MI26	06		A 2	0021	209	
										WO 2	003-	EP13	908		W 2	0031	208	

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ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): CASREACT 141:54528; MARPAT 141:54528

Page 24

The present invention discloses a process for the preparation of AR androstane-17 β -carbothioate intermediates, such as I [R = H, COR1; R1 = alkyl; R2 = H, alkyl; OR and R2 = 16a, 17a-isopropylidenedioxy, 16α , 17α -alkylidenedioxy; R4 = SCH(R3)OH; R3 = H, alkyl, (un) substituted Ph, aralkyl; X, Y and Z, in α or β position = H, OH, Cl, F, CO; X,Y = epoxy; dashed line = single or double bond], for their use in preparing 17β -fluorinated-androstane ester derivs, I (R4 = SCH(R3)F). Thus, androst-1,4-diene derivative II (R = COEt, R4 = OH), obtained by the reaction of II (R = H, R4 = OH) and propionyl chloride, was reacted with dimethylthiocarbamoyl chloride to provide dimethylthiocarbamoyl derivative II [R = COEt, R4 = SCONMe2 (III)]. Dimethylthiocarbamoyl derivative III, on treatment with phosphoric acid, provided carbothioic acid derivative II (R = COEt, R4 = SH), which upon reaction with formaldehyde and followed via selective nucleophilic fluorination, afforded 17β-fluorinated-androstane ester derivative II (R = COEt, R4 = SCH2F).

IT 80474-45-9P

CN

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PRBP (Preparation); RACT (Reactant or reagent) (preparation of 176-fluorinated-androstane esters from androstane 176-carbothioate intermediates)

RN 80474-45-9 CAPLUS

Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6a,11\(\beta\),16a,17\(\alpha\))- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L19 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:490444 CAPLUS

DOCUMENT NUMBER: 141:42892

TITLE: Thiocarboxylic acid organic salts and processes

utilizing the same

INVENTOR(S): Brand, Michael; Saeed, Shadi; Davidi, Guy; Arad, Oded

PATENT ASSIGNEE(S): Chemagis Ltd., Israel

SOURCE: U.S. Pat. Appl. Publ., 7 pp.

CODEN: USXXCO DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040116396	A1	20040617	US 2003-406310	20030404
EP 1431305	A1	20040623	EP 2003-257879	20031216
R: AT, BE, CH,	DE, DK	, ES, FR, GB	, GR, IT, LI, LU, NL,	SE, MC, PT,
IE, SI, LT,	LV, FI	, RO, MK, CY	, AL, TR, BG, CZ, EE,	, HU, SK
PRIORITY APPLN. INFO.:			IL 2002-153462	A 20021216
ASSIGNMENT HISTORY FOR U	S PATEN	T AVAILABLE	IN LSUS DISPLAY FORMA	AT
OTHER SOURCE(S):	MARPAT	141:42892		
AB The invention provi	des a t	hiocarboxyli	c acid organic amine	salts selected
from the group cons	isting	of 6,9-diflu	oro-11-hydroxy-7-prop	oionyloxy-
16α-methylpregna-3-	oxo-1,4	-diene-17-th	iocarboxylic acid	
diisopropylethylami	ne salt	, triethylam	ine salt and N-methyl	lpiperidine
salt. Fluticasone	propion	ate of high	purity is produced ac	cording to the
following steps: (1) prepa	ring a mixtu	re of the above salts	s in acetonitrile
(2) adding to this	mixture	about a two	-fold molar excess of	£

chlorofluoromethane; (3) heating the mixture at 50° for a specified period of time; (4) cooling the reaction mixture to a temperature lower than

10°; and (5) separating the precipitated crystals by filtration.

80474-45-9 RL: RCT (Reactant); RACT (Reactant or reagent)

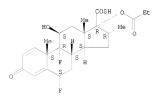
(preparation of fluticasone propionate with high purity from thiocarboxylic acid organic salts)

RN 80474-45-9 CAPLUS

Androsta-1, 4-diene-17-carbothioic acid, CN

6.9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-,

 $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA INDEX NAME)



L19 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:3108 CAPLUS

DOCUMENT NUMBER: 140:59830

TITLE: Process for preparing fluticasone propionate from

flumethasone

INVENTOR(S): Jadav, Kanaksinh Jesingbhai; Kambhampati, Sudhakar;

Chitturi, Trinadha Rao; Thennati, Rajamannar Sun Pharmaceutical Industries Limited, India

PATENT ASSIGNEE(S): PCT Int. Appl., 29 pp.

SOURCE:

CODEN: PIXXD2 DOCUMENT TYPE: Patent English

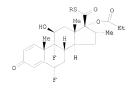
LANGUAGE: FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.											DATE						
WO	2004	0013	69		A2			1231							20030616			
		AE, CO,	AG, CR,	AL, CU,	AM, CZ,	AT, DE,	AU, DK,	AZ, DM,	BA, DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	
		LS, PH,	LT, PL,	LU, PT,	LV, RO,	MA, RU,	MD, SC,	IS, MG, SD,	MK, SE,	MN, SG,	MW, SK,	MX, SL,	MZ,	NI,	NO,	NZ,	OM,	
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		FI, BF,	FR, BJ,	GB, CF,	GR, CG,	HU,	IE, CM,	IT, GA,	LU, GN,	MC, GQ,	NL, GW,	PT, ML,	RO, MR,	SE, NE,	SI, SN,	SK, TD,	TR, TG	
IN	2003	MUOO	387		A		2005	0211							20020620 20030417			
AU	IN 216727 AU 2003263575 EP 1534733					A1 20040106				EP 2	003-	7608	56					
US	R: 2005	IE,	SI,	LT,	LV,	FI,	RO,	FR, MK, 1117	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	SK		
US	US 7208613 PRIORITY APPLN. INFO.:					B2 20070424								2	A 20020620			
															W 20030616			

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): CASREACT 140:59830

GT



Ι

AB The present invention relates to a process for preparing fluticasone propionate [I; R = CH2F (II)] via (a) treating I [R = CONMe2 (III)] with alkali metal carbonate-alc. system to obtain I [R = H (IV)]; and (b) reacting IV with bromofluoromethane. The present invention also provides an improved process for preparation of II via reacting 6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-(propionyloxy) androsta-1, 4-dien-17β-carboxylic acid with N, N-dimethylthiocarbamoyl chloride in an inert aprotic solvent in the presence of an iodide catalyst and a base to give III and then reacting III with a hydrosulfide reagent and bromofluoromethane. Thus, flumethasone on oxidation with periodic acid afforded 6α,9α-difluoro-11β,17α-dihydroxy-16α-methyl-3oxo-androst-1,4-diene-17β-carboxylic acid which was reacted with propionic anhydride to provide 6α,9α-difluoro-11β-hydroxy-16α-methyl-17α-propionyloxy-3-oxo-androst-1,4-diene-17βcarboxylic acid (V). The intermediate V was reacted with N,N-dimethylthiocarbamoyl chloride to afford III which was treated with K2CO3 in methanol to give IV. Subsequent reaction between IV and bromofluoromethane yielded II.

IT 80474-45-9P Rl: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of fluticasone propionate from flumethasone)
RN 80474-45-9 CAPLUS
Chandrosta-1.4-diene-17-carbothioic acid.

Androsta-1, 4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6α ,11 β ,1 6α ,17 α)- (CA INDEX NAME)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:633732 CAPLUS

DOCUMENT NUMBER: 139:180234

TITLE: Process for the preparation of

6α,9α-difluoro-17α-(1-oxopropoxy-

KIND DATE

11β-hydroxy-16α-methyl-3-oxo-androst-1,4-

APPLICATION NO.

DATE

diene-17β-carbothioic acid

INVENTOR(S): Coote, Steven John; Nice, Rosalvn Kav; Wipperman, Mark

David

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA	PAIENI NO.				KIND DATE			APPLICATION NO.							DAIL			
WO	2003	0666	54		A1		2003	0814			2003-				2	0030	203	
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB	, BG,	BR,	BY,	BZ,	CA,	CH,	CN,	
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC	, EE,	ES,	FI,	GB,	GD,	GE,	GH,	
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE	, KG,	KP,	KR,	KZ,	LC,	LK,	LR,	
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN	, MW,	MX,	MZ,	NO,	NZ,	OM,	PH,	
		PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK	, SL,	ΤJ,	TM,	TN,	TR,	TT,	TZ,	
								YU,										
	RW:										, TZ,							
											, CH,							
											, NL,						BF,	
											, ML,							
											2003-							
AU	2003	2068	37		A1		2003	0902		AU :	2003-	2068	37		2	0030	203	
AU	2003	2068	37		В2		2008	1113										
EP	1472	271			A1		2004	1103			2003-							
	R:										, IT,						PT,	
											TR,							
BR	2003	0073	52		A		2004	1214		BR :	2003-	7352			2	0030	203	
CN	1628	125			A		2005	0615		CN :	2003- 2003-	8032	69		2	0030	203	
JP	2005	5216	80		Т		2005	0721		JP :	2003-	5660	25		2	0030	203	
	5340 2333	44			A						2003-							
RU	2004	21/	a F		C2		2008	0910		RU .	2004- 2004-	1216	15		2	0030	203	
										ZA .	2004- 2004-	5515			2	0040	712	
	2004							1230		IN .	2004-	KNIU	42			0040	/21	
	2126 2005							0414			2004-	E006	0.4		2	0040	707	
	2005							1110			2004- 2004-							
	2004									NO.	2004-	1029			2	0040		
PRIORITY					А		2004	0501		CD .	2004- 2002-	2002			2 2			
PRIORITI	APP	LIN.	TIMEO	• •							2002- 2003-					0020		
										WU.	2003-	PLIT	TΘ		w Z	0030	203	

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 139:180234

GI

10/552,118

AB The present invention relates to a novel process for the synthesis of $6\alpha, 9\alpha-difluoro-17\alpha-(1-oxopropoxy)-11\beta-hydroxy- \\ 16\alpha-methyl-3-oxo-androst-1,4-diene-17\beta-carbothioic acid [I; R = COC2H5 [II]] or a salt thereof, useful in the preparation of anti-inflammatory steroids. Thus, I (R = H), in NN-dimethylformamide, was treated with$

propionyl chloride to afford II in 83.7% yield. IT 80474-45-9P

Ι

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of difluorooxopropoxyhydroxymethyl oxoandrostdienecarbothioic acid from difluorodihydroxymethyl oxoandrostdienecarbothioic acid)

RN 80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6\alpha,11\beta,17\alpha)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:633731 CAPLUS

DOCUMENT NUMBER: 139:180233

TITLE: Process for preparing fluticasone propionate

INVENTOR(S): Coote, Steven John; Nice, Rosalyn Kay; Wipperman, Mark

David

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 26 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.													DATE					
WO		0666	53		A2		2003	0814					20030203					
	W:	AE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,	
											EE,							
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,	
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,	
		PL,	PT.	RO.	RU,	SC.	SD,	SE,	SG,	SI,	SK,	SL,	TJ.	TM.	TN.	TR.	TT.	
											ZM.							
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,	
		KG,	KZ,	MD,	RU,	TJ,	TM.	AT,	BE.	BG,	CH,	CY.	CZ,	DE,	DK,	EE.	ES.	
		FI,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,	SK,	TR,	BF,	ВJ,	CF,	
		CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG				
CA	2473 2003	896			A1		2003	0814		CA 2	2003-	2473	896		2	0030	203	
AU	2003	2068	36		A1		2003	0902		AU 2	2003-	2068	36		2	0030	203	
AU	2003	2068	36		B2		2009	0108										
EP	1474	436			A2		2004	1110		EP 2	2003-	7045	41		2	0030	203	
EP	1474	436			B1		2009	1028										
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
		IE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	SK		
BR	2003	0072	43		A		2004	1214		BR 2	2003-	7243			2	0030	203	
JP	2005	5170	19		T		2005	0609		JP 2	2003-	5660	24		2	0030	203	
CN	1642	969			A		2005	0720		CN 2	2003-	8074	37		2	0030	203	
CN	1003	3808	7		C		2007	0919										
NZ	5343	20			A		2007	0727		NZ 2	2003-	5343	20		2	0030	203	
RU	2333	218			C2		2008	0910		RU 2	2004-	1229	28		2	0030	203	
ΑT	4469	65			T		2009	1115		AT 2	2003-	7045	41		2	0030	203	
ZA	2004	0058	26		A		2005	0811		ZA 2	2004-	5826			2	0040	721	
IN	2004	KN01	049		A		2006	0519		IN 2	2004-	KN10	49		2	0040	722	
MX	2004	0075	30		A		2004	1110		MX 2	2004-	7530			2	0040	804	
NO	2003 2005 1642 1003 5343 2333 4469 2004 2004 2004 2004 3271	0036	64		A		2004	0901		NO 2	2004-	3664			2	0040	901	
NO	3271	38			B1		2009	0504										
US	2005	0222	107		A1		2005	1006		US 2	2005-	5028	66		2	0050	502	
RIT:	Y APP	LN.	INFO	. :						GB 2	2002-	2564			A 2	0020	204	
											2003-					0030	203	

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 139:180233

AB The present invention relates to a process for preparing fluticasone propionate [I, R = CREP (II)] as crystalline polymorphic which comprises reacting I [R = H (III)] or a salt thereof with LCH2F (L = leaving group) optionally in the presence of a phase transfer catalyst, a water-immiscible non-solvating organic liquid solvent and water. Thus, $6\alpha, 9\alpha$ -difluoro-11B, 17α -dihydroxy-16\alpha-methyl-3-oxo-androst-1, 4-diene-17B-carbothioic acid was reacted with propionyl chloride to provide III which was treated with bromofluoromethane in presence of benyltributylammonium chloride and triethylamine using Et acetate as solvent and hexane as anti-solvent to afford II in 95.7% yield.

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of fluticasone propionate from difluorodihydroxymethyl oxoandrostdienecarbothioic acid)

RN 80474-45-9 CAPLUS

CN Androsta-1,4-diene-17-carbothioic acid, 6,9-diffuoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6a,11B,16a,17a)- (CA INDEX NAME)

Ι

Absolute stereochemistry. Rotation (-).

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:132962 CAPLUS

DOCUMENT NUMBER: 138:170401

TITLE: A method for preparing fluticasone derivatives
INVENTOR(S): Partridge, John Joseph; Walker, Dwight Sherod

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT	KIND DATE				APPL	ICAT		DATE							
WO 2002	013427		7.2	_	2002	0220		WO 2	002	1024	20020801				
			A3 20031016				WO Z	002-	0524	200	20020801				
	AE, AG,						D7	DD	DC.	DD	DΥ	D7	C7	CH	CN
w.															
	CO, CR,														
	GM, HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,
	LS, LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
	PL, PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TN,	TR,	TT,	TZ,
	UA, UG,	US,	UZ,	VN,	YU,	ZA,	ZM,	ZW							
RW:	GH, GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,
	KG, KZ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
	FI, FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,	SK,	TR,	BF,	BJ,	CF,
	CG, CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG			
AU 2002	321884		A1		2003	0224		AU 2	002-	3218	84		2	0020	801
PRIORITY APP						US 2	001-	3673	41P		P 2	0010	803		
								WO 2	002-	JS24	586		W 2	0020	801
OTHER SOURCE	(S):		CAS	REAC	T 13	8:17	0401								

AB A method was developed for preparing $6a, 9a-difluoro-17a-\{(2-furanylcarbonyl)oxy]-11\beta-hydroxy-16a-methyl-3-oxoandrosta-1, 4-diene-<math>\beta$ -carbothioic acid S-fluoromethyl ester by reacting the thiocarboxylic acid with a solution containing chlorofluoromethane and a mild base medium at a temperature in the range of -20° C to 60° C. Thus, the thioacid furoate I (R = H) was treated with ClCH2F in DMF containing NaI and KHCO3 at -15° for 15m and then warmed to 15°

10/552,118

≥ 15m to give 82.6 % I (R = CH2F).

IT 80474-45-9

RL: RCT (Reactant); RACT (Reactant or reagent) (method for preparing fluticasone derivs.)

RN 80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6a,17a)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

OS.CITING REF COUNT:

6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2002:90061 CAPLUS

DOCUMENT NUMBER: 136:134954

TITLE: Preparation of the anti-inflammatory steroid

intermediate 6a,9a-difluoro-

11β,17α-dihydroxy-16α-methylandrosta-

1,4-dien-3-one-17β-carboxylic acid via a novel oxidation process

INVENTOR(S): Albinson, Frederick David; Coote, Steven John; Robinson, John Malcolm
PATENT ASSIGNEE(S): Glaw Group Limited, UK

PATENT ASSIGNEE(S): Glaxo Group Limited, UK SOURCE: PCT Int. Appl., 29 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION:

PA	TENT	NO.		KIN		APE	PLIC.		DATE									
	2002				A1	_	2002	0131		WO	200	1-0	GB32	 89		2	0010	720
							AU,											
							DK.											
		GM.	HR.	HU.	ID.	IL.	IN,	IS.	JP.	KE	. к	Ġ.	KP.	KR.	KZ.	LC.	LK.	LR.
							MD,											
		RO.	RU.	SD,	SE,	SG,	SI,	SK,	SL,	TJ	J. T	м,	TR.	TT,	TZ,	UA,	UG,	US,
		UZ,	VN,	YU,	ZA,	ZW												
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ	, T	z,	UG,	ZW,	AT,	BE,	CH,	CY,
		DE,	DK,	ES,	FI,	FR,	GB,	GR,	IE,	II	r, L	U,	MC,	NL,	PT,	SE,	TR,	BF,
		BJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GV	7, M	L,	MR,	NE,	SN,	TD,	TG	
CA	2406 1301	963			A1		2002	0131		CA	200	1-	2406	963		2	0010	720
EP	1301	526			A1		2003	0416		ΕP	200	1-	9497	91		2	0010	720
EP	1301	526			B1		2008	0618										
	R:						ES,							LU,	NL,	SE,	MC,	PT,
		ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	ΑI	, T	R						
BR	2001	0104	30		A		2003	0708		BR	200	1-	1043	0		2	0010	720
HU	2003	0011	08		A2		2003		HU	200	3-	1108			2	0010	720	
HU	2003 2004 5220 2001	0011	80		A3		2008	0428										
JP	2004	5044	03		T		2004	0212		JP	200	2	5141	48		2	0010	720
NZ	5220	83			A		2004	0625		NZ	200	1-	5220	83		2	0010	720
AU	2001	2709	06		B2		2005	1013		AU	200	1-	2709	06		2	0010	720
CN	1315	864			С		2007	0210		CIA	200	T	OTTA	10		2	0.0 ± 0	120
AT	3986	28			T		2008											
IL	1523	48			A		2008											
ES	2307	628			Т3		2008	1201		ES	200	1-	9497	91		2	0010	720
ZA	1315 3986 1523 2307 2002	0083	72		A		2004	0211		ZA	200	2-	8372			2	0021	017
IN	2002	KN01	303		A		2005			IN	200	2-1	KN13	03		2		
	2002	0050	54		A		2002			ИО	200	2	5054			2	0021	021
	3248	36			B1		2007											
	7872	93			B1		2007	1220		KR	200	2-	7143	67		2	0021	025
MX	2002	0109	67		A		2003	0327		MX	200	2-	1096	7		2	0021	107
	2004	0043	974		A1		2004	0304		US	200	3-:	3335	37		2	0030	815
	1056						2009			HK	200	3-	1066	80		2	0030	917
IORIT	Y APF	LN.	INFO	.:												A 2		
																W 2	0010	720

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 136:134954

G1

AB The present invention relates to a novel oxidation process for the synthesis of a known intermediate (1), useful in the preparation of anti-inflammatory steroids. Thus, flumethasone in THF was treated with an aqueous solution of periodic acid to give I in 98% yield.

IT 80474-45-9P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of difluorodihydroxymethyl androstadienonecarboxylic acid via a novel oxidation process)

RN 80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

Ι

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, $(6\alpha,11\beta,16\alpha,17\alpha)$ - (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

INVENTOR(S):

L19 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2001:636040 CAPLUS

DOCUMENT NUMBER: 135:211173

TITLE: Method for the preparation of fluticasone and related

17β-carbothioic esters using a novel carbothioic acid synthesis and novel purification methods Barkalow, Jufang; Chamberlin, Steven A.; Cooper,

Arthur J.; Hossain, Azad; Hufnagel, John J.; Langridge, Denton C.

PATENT ASSIGNEE(S): Abbott Laboratories, USA SOURCE: PCT Int. Appl., 33 pp.

DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA	PATENT NO.					KIND DATE			APPLICATION NO.							DATE			
WO		0627	22		A3		20010830 20020516		W	0	2001-	JS60	55		2	0010223			
		AT,		CH,		DE,	DK,	ES,	FI,	FF	R, GB,	GR,	IE,	IT,	LU,	MC,	NL,		
US	2002	0133	032		A1		2002	0919	U	S	2000-	5133	99		2	0000	225		
CA	2400	919			A1		2001	0830	C.	Α	2001-	2400	919		2	0010	223		
CA	2400 2400	919			С		2009	0120											
EP	1257	531			A2		2002	1120	E	Ρ	2001-	9162	31		2	0010	223		
EP	1257	531			B1		2004	0915											
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GF	, IT,	LI,	LU,	NL,	SE,	MC,	PT,		
					TR														
JP	2003 3986	5295	64		T		2003	1007	J	Ρ	2001-	5617	31		2	0010	223		
JP	3986	313			B2		2007												
AT	2762	35			T		2004				2001-								
	1257							0131	P	Т	2001-	9162	31		2	0010	223		
ES	2228	832			Т3		2005	0416	E	S	2001-	9162	31		2	0010:	223		
CN	1381	444			A		2002	1127	C	N	2001-	1196	71		2	0010	419		
IN	2001	MUOO	632		A		2005	0819	I	N	2001-1	MU63:	2		2	0010	706		
MX	2002	0082	75		A		2003				2002-					00208	323		
US	2004	0209	854		A1			1021	U	S	2004-	8478	46		2	0040	518		
US	7214	807			B2		2007	0508											
PRIORIT	Y APP	LN.	INFO	. :					U	S	2000-	5133	99	Z	2	0000	225		
											2001-					0010:	223		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): CASREACT 135:211173; MARPAT 135:211173

GI

AB A method for converting a carboxylic acid to a carbothioic acid group I (R and Rl independently are Cl-6 alkyl or R and Rl independently are Cl-6 alkylene) was accomplished. This method was used for the conversion of carboxylic acids to carbothioic acids, and for both the preparation of androstane 179-carbothioic acids and fluticasone propionate which avoided the use of column chromatog. Thus II was prepared from flumethasone reacted in Pd(II) acetate and PPh3 in DMA yielding the 179-carboxylic acid which was treated with propionyl chloride followed by N,N-dimethylthiocarbamoyl chloride and then chlorofluoromethane yielding II in 70%.

ΙI

- IT 80474-45-9DP, salts
 RL: SPN (Synthetic preparation); PREP (Preparation)
- (preparation of androstane 17β-carbothioic esters) RN 80474-45-9 CAPLUS
- CN Androsta-1, 4-diene-17-carbothioic acid,
 - 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6\alpha,11\beta,17\alpha)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

- OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
- REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1999:48734 CAPLUS

DOCUMENT NUMBER: 130:110460

TITLE: Therapeutically active compounds hydrolyzable in human

or animal blood to compounds with reduced therapeutic

activity

INVENTOR(S): Biggadike, Keith; Angell, Richard Martyn; Procopiou,
Panaviotis Alexandrou; Farrell, Rosanne Mary; Ramesh,

Usha V.; Holmes, Duncan Stuart

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.							DATE			APF	LICAT	ION	NO.		DATE			
		9901 9901				A2					WO	1998-	EP39	05		1	9980	626	
		W:	DK, KP, NO,	EE, KR, NZ,	ES, KZ, PL,	FI, LC, PT,	GB, LK, RO,	GE, LR,	GH, LS, SD,	GM, LT,	GW	R, BY, I, HU, I, LV, G, SI,	ID, MD,	IL, MG,	IS, MK,	JP, MN,	KE, MW,	KG, MX,	
		RW:	GH, FI,	GM, FR,	KE, GB,	LS, GR,	MW, IE,	SD,	SZ, LU,	MC,	NL	, AT, , PT,							
	EP	9984	84			A1		2000	0510		ΕP	1998-	9349	98		1	9980	626	
	EP	9984	84			B1		2004	0303										
		R:							FR,	GB,	GF	, IT,	LI,	LU,	NL,	SE,	MC,	PT,	
				SI,															
												1999-							
	JΡ	2002 2609	3221	68		A		2002	1108			2002-							
	ΑT	2609	31			T		2004	0315			1998-					9980	626	
								2004	1001		ES	1998-	9349	98		1	9980	626	
		2002						2002				2000-							
	US	2005	0070	515		A1		2005	0331			2003-				2	0030	807	
PRIOR	RIT:	Y APP	LN.	INFO	. :							1997-					9970		
											GB	1997-	1381	9			9970		
											JP	1999-	5062	77		A3 1	9980	626	
												1998-					9980		
											US	2000-	4465	85		A3 2	0000	211	

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): MARPAT 130:110460

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

GI

AB Herein are described therapeutically active compds. hydrolyzable in human or animal blood to compds. with reduced therapeutic activity with the proviso that the therapeutically active compound is not selected from steroids I [R1 = 0, 5, NH; R2 = OC(:0)C1-6-alkyl; R3 = H, α -,

 $\beta\text{-Me},$ methylene; R2R3 = OCR6R7O; R4, R5 = H, halogen; R6, R7 = H, C1-6-alkyl; dashed line = single or of ouble bond], II and III. There is also described a method of identifying a compound capable of providing a therapeutic effect at a target site within a human or animal body with reduced systemic potency to said body comprising evaluating the half-life of said compound in the presence of human serum paraoxonase, where the suitable compds. have a half-life of less than 1 h. Thus, spiroandrostadiene IV was prepared from carbothioioc acid V via cyclization with 1,1'-carbonyldimidazole in DMF. Spiroandrostadiene IV had an EC50 < 250 nM in the glucocorticosteroid assay, while dihydrofuranone VI-C3CO2H was found to be 5.3 more active than isoprenaline as a $\beta\text{--}$ 2-arenoreceptor agonist.

IT 80474-45-9

RL: RCT (Reactant); RACT (Reactant or reagent)

11

(preparation of glucocorticosteroid derivs. as β 2-adrenoreceptor agonists)

RN 80474-45-9 CAPLUS CN Androsta-1.4-diene

Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6a,11B,16a,17a)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

OS.CITING REF COUNT:

- THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
- REFERENCE COUNT:
- 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/552,118

L19 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1998:706263 CAPLUS DOCUMENT NUMBER: 129:276096

DOCUMENT NUMBER: 129:276096 ORIGINAL REFERENCE NO.: 129:56305a

TITLE: Process for the manufacture of

androstane-17-carbothioates via esterification with

halofluoromethanes
INVENTOR(S): Cherkez, Stephen

PATENT ASSIGNEE(S): Chemagis Ltd., Israel

SOURCE: Israeli, 15 pp.
CODEN: ISXXAQ

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IL 109656	A	19980222	IL 1994-109656	19940515
IN 185691	A1	20010407	IN 1994-DE1716	19941230
PRIORITY APPLN. INFO.:			IL 1994-109656 F	19940515
OTHER SOURCE(S):	CASREA	CT 129:27609	6; MARPAT 129:276096	

0 SR1
HO Me OR2
R3

- AB A process for the preparation of an androstane-17-carbothicic ester I (R1 = fluoromethyl, difluoromethyl, trifluoromethyl, R2 = COR6, R6 = C1-3-alkyl, R3 = H, α-Me, β-Me, methylene; R = H, Cl, F; R5 = H, F; dotted line = single or double bond) by the direct esterification of a corresponding androstane-17-carbothicic acid I (R1 = H] with a halofluoromethane of formula XCH2F, XCH2P or XCF3 [X = Br, Cl] and optionally in the presence of a catalyst is claimed. Thus, fluticasone propionate (I; R1 = CH2F, R2 = COSt, R3 = Me, R4 = R5 = Me, dashed line = double bond) was prepared via esterification of I (R1 = H, R2 = COSt, R3 = Me, R4 = R5 = Me, dashed and catalytic Bu4Mbr.
- IT 80474-45-9

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of androstane-17-carbothioates via esterification with halofluoromethanes)

- RN 80474-45-9 CAPLUS
- CN Androsta-1, 4-diene-17-carbothioic acid,
 - 6,9-difluoro-11-hydroxy-16-methy1-3-oxo-17-(1-oxopropoxy)-,

 $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

L19 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1997:481001 CAPLUS DOCUMENT NUMBER: 127:95450

ORIGINAL REFERENCE NO.: 127:18385a,18388a

TITLE: Preparation of lactone derivatives of

17β-carboxy, carbothio and amide androstane derivatives

INVENTOR(S): Biggadike, Keith; Procopiou, Panaviotis Alexandrou

PATENT ASSIGNEE(S): Glaxo Group Limited, UK SOURCE: PCT Int. Appl., 63 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

P	'ΑΊ	ENT	NO.			KIN	D	DATE			API	PL1	CAT	ION	NO.		Ι	ATE	
								1997											
		W:	AL.	AM.	AT.	AU,	AZ.	BA,	BB,	BG,	BE	٦,	BY,	CA.	CH,	CN.	CU.	CZ.	DE,
			DK.	EE.	ES.	FI.	GB.	GE.	HU.	IL.	13	s.	JP.	KE.	KG.	KP.	KR.	KZ.	LC.
			LK.	LR.	LS.	LT.	LU.	LV,	MD.	MG.	ME	ĸ.	MN.	MW.	MX.	NO.	NZ.	PL.	PT.
			RO,	RU.	SD,	SE.	SG,	SI,	SK.	TJ.	Th	4.	TR.	TT.	UA.	UG,	US.	UZ,	VN
		RW:						UG,											
			IE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	Bo	J,	CF,	CG,	CI,	CM,	GA,	GN,	ML,
			MR.	NE,	SN,	TD,	TG												
		2241				A1		1997	0710		CA	19	96-	2241	728		1	9961	219
A	U	9711	409			A		1997	0728		AU	19	97-	1140	9		3	9961	219
A	U	7218	65			B2		2000	0713										
E	ΣP	8763	92			A1		1998 2000	1111		EP	19	96-	9424	93		1	9961	219
E	ΣP																		
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GE	٦,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
			IE,	SI,	LT,	LV,	FI,	RO											
J	ſΡ	1150	1675			T		1999 1999 1999 2004 1999 2000 2000 2000 2000 2000 2000 2000	0209		JΡ	19	96-	5240	95		3	9961	219
J	ſΡ	2947	944			B2		1999	0913										
C	N	1209	135			A		1999	0224		CN	19	96-	1801	07		1	9961	219
C	N	1133	643			С		2004	0107										
E	3R	9612	309			A		1999	0713		BR	19	996-	1230	9		1	9961	
H	IU	9903	707			A2		2000	0328		HU	19	99-	3707			1	9961	219
Н	U	9903	707			A3		2000	0428										
A	ıΤ	1943	56			T		2000	0715		ΑT	19	996-	9424	93		3	9961	
E	S	2150	150			Т3		2000	1116		ES	19	96-	9424	93		1	9961	
P	'Τ	8763	92			Е		2000	1229		PT	19	996-	9424	93		3	9961	
I	'W	4980	72			В		2000 2002 2005 2001 1998	0811		TW	19	997-	8610	8975		1	9970	
1	N.	1997	CAUI	233		A		2005	0311		IN	19	997-0	CA12	33		1	9970	
U	JS	6197 9803	761			B1		2001	0306		US	19	998-	9174	8]	9980	
4	10	9803	004			A		1998	0826		NO	15	998-	3004			1	9980	626
4	10	3110	22			BI		2001	1001										
		1012				A1		2001 2001	0123		HK	15	198-	1136	83		1	9981	216
		3034				13		2001	0131		GR	20	100-	4022	54			0001	004
PRIORI	1.7	APP	PM.	TMEO	. :						GB	15	193-	2005	1		A J	9951	
															1			9960	
											WO	15	196ー	GB31	4 U		W J	9961	219

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 127:95450

AB Title compds. I [R1 = 0, S, NH; R2 = OCO-C1-6 alkyl; R3 = H, Me, CH2; or R2R3 = bond, $^{-O}-CGR6R^{-O}-F,R6$, R7 = H, alkyl; R4, R5 = H, halo] and their solvates, useful as anti-inflammatory or anti-allergic agents, are prepared Thus, 6α , 9α -difluoro- 11β -hydroxy- 16α -methyl-3-oxo- 17α -propionyloxyandrosta-1, 4-diene- 17β -carbothioic acid was reacted with α -bromo-y-butyrolactone in DMF containing K2CO3 to give both the 3(S)-S- (main product) and the 3(R)-S-(2-oxotetrahydrofuryl)ester. In an in vitro study using Hela cells transfected with detectable reporter gene (secreted placental alkaline phosphatase, SPAP), these had an EC50 of <400 nM. Pharmaceutical compns. containing I are described.

Ι

80474-45-9

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of lactone derivs. of 17β-carboxy, carbothio and amide androstane derivs.)

RN 80474-45-9 CAPLUS

CN Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6a,11B,16a,17a)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

```
L19 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:
                        1995:64934 CAPLUS
DOCUMENT NUMBER:
                        122:81726
ORIGINAL REFERENCE NO.: 122:15539a,15542a
                        Synthesis and Structure-Activity Relationships in a
TITLE:
                        Series of Antiinflammatory Corticosteroid Analogs,
                        Halomethyl Androstane-17β-carbothioates and
                        -17B-carboselenoates
AUTHOR(S):
                        Phillipps, Gordon H.; Bailev, Esme J.; Bain, Brian M.;
                        Borella, Raymond A.; Buckton, Jacky B.; Clark, John
                        C.; Doherty, Alice E.; English, Alan F.; Fazakerley,
                        Harold; et al.
CORPORATE SOURCE:
                        Glaxo Research and Development Limited, Greenford/
                        Middlesex, UB6 OHE, UK
                        Journal of Medicinal Chemistry (1994), 37(22), 3717-29
SOURCE:
                        CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE:
                        Journal
LANGUAGE:
                        English
    The preparation and topical antiinflammatory potencies of a series of
     halomethyl 17a-(acyloxy)-11B-hydroxy-3-oxoandrosta-1,4-diene-
     17β-carbothicates, carrying combinations of 6α-fluoro,
     9a-fluoro, 16-Me, and 16-methylene substituents, are described. Key
     synthetic stages were the preparation of carbothioic acids and their reaction
     with dihalomethanes. The carbothioic acids were formed from
     17β-carboxylic acids by initial reaction with dimethylthiocarbamoyl
     chloride followed by aminolysis of the resulting rearranged mixed
     anhydride with diethylamine, or by carboxyl activation with
     1,1 -carbonyldiimidazole (CDI) or 2-fluoro-N-methylpyridiniumtosylate
     (FMPT) and reaction with hydrogen sulfide, the choice of reagent being
     governed by the 17a-substituent. Carboxyl activation with FMPT and
     reaction with sodium hydrogen selenide led to the halomethyl
     16-methyleneandrostane-17β-carboselenoate analogs. Antiinflammatory
     potencies were measured in humans using the vasoconstriction assay and in
     rats and mice by a modification the Tonelli croton oil ear assay. Best
     activities were shown by fluoromethyl and chloromethyl carbothioates with
     a 17a-propionyloxy group. S-Fluoromethyl
     6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-
     17α-(propionyloxy)androsta-1,4-diene-17β-carbothioate
     (fluticasone propionate, FP) was selected for clin. study as it showed
     high topical antiinflammatory activity but caused little
     hypothalamic-pituitary-adrenal suppression after topical or oral
     administration to rodents.
IΤ
    80474-45-9P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (synthesis and structure-activity relationships in a series of
       antiinflammatory corticosteroid analogs and halomethyl
       androstane-17β-carbothioates and -17β-carboselenoates)
     80474-45-9 CAPLUS
RN
CN
    Androsta-1, 4-diene-17-carbothioic acid,
     6,9-difluoro-11-hvdroxy-16-methv1-3-oxo-17-(1-oxopropoxy)-,
     (6α, 11β, 16α, 17α) - (CA INDEX NAME)
```

Absolute stereochemistry. Rotation (-).

OS.CITING REF COUNT: 32 THERE ARE 32 CAPLUS RECORDS THAT CITE THIS RECORD (32 CITINGS)

10/552,118

L19 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1987:5327 CAPLUS DOCUMENT NUMBER: 106:5327

ORIGINAL REFERENCE NO.: 106:999a,1002a

TITLE: Androstane carbothioates

INVENTOR(S): Phillipps, Gordon H.; Bain, Brian M.; Williamson,

Christopher; Steeples, Ian P.
PATENT ASSIGNEE(S): Glaxo Group Ltd., UK

SOURCE: Can., 22 pp. Division of Can. Appl. No. 370,853.

CODEN: CAXXA4

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
CA 1205464	A2	19860603	CA 1985-476250		19850311
US 4335121	A	19820615	US 1981-234113		19810213
ZA 8100976	A	19820728	ZA 1981-976		19810213
CH 651307	A5	19850913	CH 1984-3890		19810213
CA 1201114	A1	19860225	CA 1981-370853		19810213
GB 2137206	A	19841003	GB 1983-25400		19830922
GB 2137206	В	19850403			
AT 8400170	A	19920515	AT 1984-170		19840119
AT 395428	B	19921228			
AT 8602031	A	19920515	AT 1986-2031		19860728
AT 395429	В	19921228			
AT 9100344	A	19960215	AT 1991-344		19910219
AT 401521	В	19960925			
PRIORITY APPLN, INFO.:			GB 1980-5174	A	19800215
			CA 1981-370853	A3	19810213
			GB 1980-13339	A	19800423
			AT 1981-674	Α	19810213
			CH 1981-982	A	19810213
			GB 1981-4496	A3	19810213

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Title compds. I (R1 = CH2F, CH2Cl, CH2Br, CH2CH2F; R2 = alkanoyl; R3 = H, α -Me, β -Me, :CH2; R2R3 = α , α -CMe2O; R4 = H, Cl, F; R5 = H, F; A1 may be present or absent) are prepared as

antiinflammatory agents. Thus, androstadienone derivative II (R6 = R7 = OH) was treated with EtCOCl to give II (R6 = O2CBt, R7 = OH), which was treated with Et3N and Me2NCSCl to give II (R6 = O2CBt, R7 = OCSNMe2). Rearrangement and aminolysis in refluxing Et2NH gave II (R6 = O2CBt, R7 = SH), which was alkylated by BrCR2Cl to give II (R6 = O2CBt, R7 = SCH2Cl), a preferred compound I show good topical antiinflammatory activity by the McKenzie patch test in man, and by reduction of croton oil-induced edema in mice and rats; some I show minimal hypothalmic/oituitary/darenal-suppressive activity as well (no data).

IT 80474-45-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and chloromethylation of)

RN 80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6α,11β,16α,17α)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L19 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1982:163044 CAPLUS DOCUMENT NUMBER: 96:163044

ORIGINAL REFERENCE NO.: 96:26859a,26862a

Androstane carbothioates PATENT ASSIGNEE(S): Glaxo Group Ltd., UK SOURCE: Neth. Appl., 63 pp.

CODEN: NAXXAN DOCUMENT TYPE: Patent LANGUAGE: Dutch

FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION:

PAT	TENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL	8100707	A	19810916	NL 1981-707	19810213
	191792	В	19960401		25020020
	191792	Ċ	19960802		
	887518	A1	19810813	BE 1981-203794	19810213
	8100623	A	19810816	DK 1981-623	19810213
	147022	В	19840319	DI 1301 010	13010110
	147022	c	19840827		
	8100444	A	19810816	FI 1981-444	19810213
	70904	В	19860718		
	70904	c	19861027		
	8101010	A	19810816	SE 1981-1010	19810213
	452468	В	19871130		
	452468	c	19880310		
	8167298	Ā	19810820	AU 1981-67298	19810213
	544517	B2	19850606		
	2477156	A1	19810904	FR 1981-2818	19810213
	2477156	B1	19841116		
	56138200	A	19811028	JP 1981-20790	19810213
	63037120	В	19880722		
DE	3105307	A1	19811210	DE 1981-3105307	19810213
	3105307	C2	19880929		
US	4335121	A	19820615	US 1981-234113	19810213
GB	2088877	A	19820616	GB 1981-4496	19810213
GB	2088877	В	19840704		
ZA	8100976	A	19820728	ZA 1981-976	19810213
CH	644615	A5	19840815	CH 1981-982	19810213
CH	651307	A5	19850913	CH 1984-3890	19810213
AT	8100674	A	19920515	AT 1981-674	19810213
AT	395427	В	19921228		
DE	3153379	C2	19921119	DE 1981-3153379	19810213
FR	2485542	A1	19811231	FR 1981-15812	19810817
FR	2485542	B1	19830610		
US	4578221	A	19860325	US 1983-513396	19830714
GB	2137206	A	19841003	GB 1983-25400	19830922
GB	2137206	В	19850403		
AT	8400170	A	19920515	AT 1984-170	19840119
AT	395428	В	19921228		
US	4650610	A	19870317	US 1985-753428	19850710
AT	8602031	A	19920515	AT 1986-2031	19860728
AT	395429	В	19921228		
	9100344	A	19960215	AT 1991-344	19910219
AT	401521	В	19960925		

SK 278140 CZ 281275 PRIORITY APPLN. INFO.:	B6 B6	19960207 19960814	CZ GB GB AT CH GB US	1991-4034 1991-4034 1980-5174 1980-13339 1981-674 1981-982 1981-4496 1981-256845	A3 A1	19911223 19911223 19800215 19800423 19810213 19810213 19810213 19810423
				1982-408837		19820817
			US	1983-513396	A1	19830714

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): CASREACT 96:163044; MARPAT 96:163044 GI

- AB Antinflammatory (no data) androstanes I (R = CH2F, CH2C1, CH2Br, CH2CH2F; R1 = acyl; R1R2 = CH2O; R2 = H, α or β -Me, R7 = H; R2R7 = CH2; R3 = H, C1, F; R4 = H, F; R5 = R6 = H; R5R6 = bond) were prepared Thus, I (R = CH2C1, R1 = COEt, R2 = β -Me, R3 = F, R4 = H, R5R6 = bond, R7 = H) was prepared by treating the corresponding 17-carboxylic acid with Me2NCSC1, hydrolyzing to the 17-thiocarboxylic acid, and esterifying with BFCH2C1. IT 80474-45-9P
- Rl: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 - (preparation and esterification of)
- RN 80474-45-9 CAPLUS
- CN Androsta-1, 4-diene-17-carbothioic acid,
 6, 9-diffluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-,
 (6a, 11B, 16a, 17a) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

OS.CITING REF COUNT: 29 THERE ARE 29 CAPLUS RECORDS THAT CITE THIS RECORD (31 CITINGS)

the name of the request. To delete a component from the multifile SDI, enter <code>DELETE</code> and the name of the component.

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L3 6 S 5-6-6-6/SZ AND L2 L4 11 S L2 NOT L3

L5 17324 S 4432.3.25/RID L6 902 S CARBOTHIO? AND L5

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L8 50 S L7

L9 4352 S L7 SSS FUL L10 STRUCTURE UPLOADED L11 1945 S L10 SUB=L9 FUL

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FILE 'CAPLUS' ENTERED AT 12:14:38 ON 01 JUN 2010 L14 45 S L13

L15 35 S L3 AND L14

FILE 'REGISTRY' ENTERED AT 12:14:59 ON 01 JUN 2010 L16 21 S C24 H30 F2 O5 S/MF

L17 1 S L16 AND L3 FILE 'CAPLUS' ENTERED AT 12:15:24 ON 01 JUN 2010

28 S L17 25 S L18 NOT (2010/SO OR 2009/SO OR 2008/SO OR 2007/SO OR 2006/SO

FILE 'REGISTRY' ENTERED AT 12:21:15 ON 01 JUN 2010

FILE 'CASREACT' ENTERED AT 12:24:26 ON 01 JUN 2010

FILE 'REGISTRY' ENTERED AT 12:24:55 ON 01 JUN 2010

FILE 'CAPLUS' ENTERED AT 12:25:06 ON 01 JUN 2010 L20 15989 S CARBODIIMIDE

L21 1 S L12 AND L20

L21 1 5 L12 AND L20 L22 1862 S L3 NOT L17

L23 ANALYZE L22 1- RN HIT : 5 TERMS

L18

L19

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FILE 'REGISTRY' ENTERED AT 12:27:52 ON 01 JUN 2010
L24 1 S 80474-14-2/RN
L25
            1 S 2135-17-3/RN
L26
            1 S 28416-82-2/RN
L27
            1 S 65429-42-7/RN
L28
            1 S 73205-13-7/RN
   FILE 'CAPLUS' ENTERED AT 12:29:04 ON 01 JUN 2010
L29
         1434 S L24
L30
           14 S L28
L31
            1 S L20 AND L29
L32
            1 S L20 AND L30
L33
            37 S L24/P
L34
            6 S L28/P
L35
            41 S L33 OR L34
L36
            20 S L19 AND L35
L37
            41 S L35 OR L36
L38
            39 S L37 NOT (2010/SO OR 2009/SO OR 2008/SO OR 2007/SO OR 2006/SO
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=> d ibib abs hitstr total

L38 ANSWER 1 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2010:621494 CAPLUS

TITLE: Preparation for local administration containing

fluticasone propionate

INVENTOR(S): Nagao, Takeshi; Kagami, Kazuhiro; Ogawa, Taisuke
PATENT ASSIGNEE(S): Aska Pharmaceutical Co., Ltd., Japan; Galeni Search

Laboratories

SOURCE: Jpn. Kokai Tokkyo Koho, 13pp.

DOCUMENT TYPE: CODEN: JKXXAF
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT	NO.			KIN	D	DATE			APPL	ICAT	ION	NO.		D	ATE	
JP 201					-	2010	0.5.2.0			008-					0081	
														_		
WO 201				A1		2010									0091	
W:	AE	AG,	AL,	AM,	AO,	ΑT,	AU,	AZ,	BA,	BB,	BG,	BH,	BR,	BW,	BY,	ΒZ,
	CA	CH,	CL,	CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DO,	DZ,	EC,	EE,	EG,
	ES	FI,	GB,	GD,	GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	IL,	IN,	IS,	KE,
	KG	KM,	KN,	KP,	KR,	KZ,	LA,	LC,	LK,	LR,	LS,	LT,	LU,	LY,	MA,	MD,
	ME	MG,	MK,	MN,	MW,	MX,	MY,	MZ,	NA,	NG,	NI,	NO,	NZ,	OM,	PE,	PG,
	PH	PL,	PT,	RO,	RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	ST,	SV,	SY,
	TJ	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	ZA,	ZM,	ZW	
RW	: AT	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HR,	HU,
	IE	IS,	IT,	LT,	LU,	LV,	MC,	MK,	MT,	NL,	NO,	PL,	PT,	RO,	SE,	SI,
	SK	SM,	TR,	BF,	BJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,
	SN	TD,	TG,	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,
	ZM	ZW,	AM,	AZ,	BY.	KG,	KZ.	MD.	RU,	TJ.	TM					

PRIORITY APPLN. INFO.: JP 2008-283080 A 20081104

AB Disclosed are fluticasone propionate microparticles useful as active ingredients for a preparation for local administration which enables the long-term retention of microparticles of an active ingredient in a mucosa for a long period to achieve a higher therapeutic effect and a higher long-acting property, each of which comprises a fluticasone propionate crystal core and needle-like fluticasone propionate crystals which have been grown radially around the crystal core and which has an average particle size of 10 to 60 µm. Thus, fluticasone propionate crystal microparticle of the present invention (average particle size of 30-50 µm) was prepared by dissolving fluticaone propionate in ethanol, applying a nuclear particle of fluticasone propionate, and gradually adding water thereto. The microparticle attached well to the nasal mucosa in rats.

IT 80474-14-2P

RL: PEP (Physical, engineering or chemical process); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(preparation for local administration containing fluticasone propionate) ${\rm RN} = 80474-14-2 \ {\rm CAPLUS}$

CN Androsta-1,4-diene-17-carbothioic acid,
6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-,
S-(fluoromethyl) ester. (6a.118,16a.17a)- (CA

INDEX NAME)
Absolute stereochemistry.



L38 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2010:597858 CAPLUS

DOCUMENT NUMBER: 152:534698

TITLE: Preparation for local administration containing

fluticasone propionate

INVENTOR(S): Nagao, Takeshi; Kagami, Kazuhiro; Ogawa, Yasuaki

PATENT ASSIGNEE(S): JGC Corp., Japan PCT Int. Appl., 23pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LAI

FAMI	UAGE: LY ACC. NUM. COUNT: NT INFORMATION:	Japanese 2		
	PATENT NO.		APPLICATION NO.	
	WO 2010052896	A1 20100514		20091104
			DE, DK, DM, DO, DZ	
			HN, HR, HU, ID, IL	
			LK, LR, LS, LT, LU	
			NA, NG, NI, NO, NZ	
			SE, SG, SK, SL, SM	
			US, UZ, VC, VN, ZA	
			EE, ES, FI, FR, GB	
			MT, NL, NO, PL, PT CM, GA, GN, GQ, GW	
			MW, MZ, NA, SD, SL	
		AZ, BY, KG, KZ, MD,		, 65, 15, 66,
	JP 2010111592			20081104
PRIO	RITY APPLN. INFO.:		JP 2008-283080	
AB	Disclosed are flutic			
	ingredients for a pr			
	long-term retention			
	for a long period to long-acting property			
	crystal core and nee			
	been grown radially			
	size of 10 to 60 µm.			
	microparticle of the			
	was prepared by diss	olving fluticaone p	ropionate in ethano	l, applying a
	nuclear particle of			
	thereto. The microp		ll to the nasal muc	osa in rats.
IT	80474-14-2P, Flutica			
	RL: PEP (Physical, e			
	(Purification or rec study); PREP (Prepar			iological
			n containing flutic	acono propionato)
RN	80474-14-2 CAPLUS	iocai auministratio	m concarning fructe	asone propionate)
CN	Androsta-1, 4-diene-1	7-carbothioic acid.		
	6,9-difluoro-11-hvdr			,
	C-(fluoromothyl) cat			•

INDEX NAME) Absolute stereochemistry.

S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA

16

REFERENCE COUNT:

THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:1191620 CAPLUS

DOCUMENT NUMBER: 151:358973

TITLE: Process for the preparation of

androstadienecarbothioates

INVENTOR(S): Malanga, Franço; Pozzoli, Claudio Gianluca

PATENT ASSIGNEE(S): Farmabios S.p.A., Italy

SOURCE: Ital. Appl., 21pp. CODEN: ITXXCZ

DOCUMENT TYPE: Patent.

LANGUAGE: Italian FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
21122112 1101		21112	111111111111111111111111111111111111111	21112
IT 2005MI2419 IT 1366982	A1 B1	20060320	IT 2005-MI2419	20051220
PRIORITY APPLN. INFO.: OTHER SOURCE(S):			IT 2005-MI2419 73; MARPAT 151:358973	20051220
GT	CASKE	401 131:3309	73; MARPAI 131:330973	

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

ΔR A process for the preparation of androstadienecarbothicates I [R1 = COR7; R2 = H, α - or β -Me, CH2; OR1R2 = isopropylidenedioxy; R3 = OH; R4 = H, α -halogen; R3R4 = β -epoxide; R5 = H, haloge; R6 = C1, Br, F; R7 = C1-3-alkyl; dashed line = single or double bond] from the corresponding (N, N-dimethylcarbamoyl)thiocarbonyl derivs. II is described. The process comprises reaction of II with HNR8R9 [R8, R9 = linear or branched C2-6-alkyl, C5-6-cycloalkyl] followed by reaction with XCH2R6 [X = Cl, Br, mesylate, tosylate, trifluoromethanesulfonate]. Thus, fluticasone propionate (III) was prepared from 17β-[(N,N-Dimethylcarbamoyl)thiocarbonyl]-6α,9α-difluoro-11β-hydroxy-16α-methyl-17α-propionyloxy-3-oxoandrosta-1,4diene (IV) via sequential treatment with HNEt2 followed by BrCH2F in DMF containing Et3N.

80474-14-2P, Fluticasone propionate

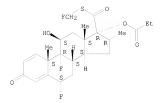
RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of androstadienecarbothicates from (N, N-dimethylcarbamovl)thiocarbonvl derivs.)

80474-14-2 CAPLUS RN

Androsta-1, 4-diene-17-carbothioic acid, CN

> 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA

INDEX NAME)



10/552,118

L38 ANSWER 4 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:131178 CAPLUS

DOCUMENT NUMBER: 150:214576

TITLE: Process for refining Fluticasone propionate

INVENTOR(S): Liu, Baofeng; Yang, Fuzhen; Xu, Baoying; Hu, Jianying PATENT ASSIGNEE(S): Tianjin Central Pharmaceutical Co., Ltd., Peop. Rep.

China

SOURCE: Faming Zhuanli Shenging Gongkai Shuomingshu, 7pp.

CODEN: CNXXEV

DOCUMENT TYPE: Patent LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 101353367	A	20090128	CN 2008-10151322	20080916
RIORITY APPLN. INFO.:			CN 2008-10151322	20080916
B Fluticacone proping	ata wac	refined by	alc and actor mixed	colvent via

AB Fluticasone propionate was refined by alc. and ester mixed solvent via recrystn. The alc. was selected from methanol, ethannol, and propanol. The seter was chosen from Et acetate, Me acetate, or Pr acetate.

80474-14-2P, Fluticasone propionate

RL: PUR (Purification or recovery); PREP (Preparation) (refining Fluticasone propionate by recrystn.)

RN 80474-14-2 CAPLUS

N Androsta-1,4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-,

S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA

INDEX NAME)

L38 ANSWER 5 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:1536347 CAPLUS

DOCUMENT NUMBER: 150:64058

TITLE: Deuterium-enriched fluticasone propionate for treating

asthma, allergic rhinitis, eczema, and psoriasis

INVENTOR(S): Czarnik, Anthony W. PATENT ASSIGNEE(S): Protia, LLC, USA

U.S. Pat. Appl. Publ., 7pp. SOURCE:

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT	INFORMATION:

	TENT :				KIN)	DATE		- 1	APPL	ICAT	ION	NO.		D.	ATE	
	2008				A1	-	2008	1225	,	JS 2	007-	7656	57		2	0070	620
WO	2008	1576	52		A1		2008	1224	1	70 2	008-	JS67	422		2	0800	619
	W:	ΑE,	AG,	AL,	AM,	AO,	ΑT,	AU,	AZ,	BA,	BB,	BG,	BH,	BR,	BW,	BY,	BZ,
		CA,	CH,	CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DO,	DZ,	EC,	EE,	EG,	ES,
		FI,	GB,	GD,	GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,
		KG,	KM,	KN,	KΡ,	KR,	ΚZ,	LA,	LC,	LK,	LR,	LS,	LT,	LU,	LY,	MA,	MD,
		ME,	MG,	MK,	MN,	MW,	MX,	MY,	MZ,	NA,	NG,	NI,	NO,	NZ,	OM,	PG,	PH,
		PL,	PT,	RO,	RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	SV,	SY,	TJ,	TM,
		TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	ZA,	ZM,	ZW			
	RW:	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HR,	HU,
		IE,	IS,	IT,	LT,	LU,	LV,	MC,	MT,	NL,	NO,	PL,	PT,	RO,	SE,	SI,	SK,
		TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,
		TG,	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,
		AM,	AZ,	BY,	KG,	KZ,	MD,	RU,	TJ,	TM							
(IT	APP	LN.	INFO	. :					1	US 2	007-	7656	57		A 2	0070	620

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 150:64058

AB The present application describes deuterium-enriched fluticasone propionate, pharmaceutically acceptable salt forms thereof, and methods of treating using the same. In the examples, four deuterium-enriched fluticasone propionate compds. are presented, and a synthesis scheme is

provided. 80474-14-2DP, Fluticasone propionate, deuterium-enriched

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(deuterium-enriched fluticasone propionate for treating asthma, allergic rhinitis, eczema, and psoriasis)

80474-14-2 CAPLUS RN

Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA

INDEX NAME)



L38 ANSWER 6 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:1531501 CAPLUS

DOCUMENT NUMBER: 150 - 64039

TITLE: Deuterium-enriched fluticasone propionate for treating

asthma, allergic rhinitis, eczema, and psoriasis

INVENTOR(S): Czarnik, Anthony PATENT ASSIGNEE(S): Protia LLC, USA

SOURCE: PCT Int. Appl., 19pp.

CODEN: PIXXD2 DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION:

	PATENT NO.					KIND DATE				ICAT	DATE					
	WO 2008157652				A1 20081224							20080619				
W	AE,	AG,	AL,	AM,	AO,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BH,	BR,	BW,	BY,	BZ,
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	FI,	GB,	GD,	GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,
	KG,	KM,	KN,	KP,	KR,	ΚZ,	LA,	LC,	LK,	LR,	LS,	LT,	LU,	LY,	MA,	MD,
	ME,	MG,	MK,	MN,	MW,	MX,	MY,	ΜZ,	NA,	NG,	NΙ,	NO,	NZ,	OM,	PG,	PH,
	PL,	PT,	RO,	RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	SV,	SY,	TJ,	TM,
	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	ZA,	ZM,	ZW			
RI	: AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FΙ,	FR,	GB,	GR,	HR,	HU,
	IE,	IS,	IT,	LT,	LU,	LV,	MC,	MT,	NL,	NO,	PL,	PT,	RO,	SE,	SI,	SK,
	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,
	TG,	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,
	AM,	AZ,	ΒY,	KG,	ΚZ,	MD,	RU,	ΤJ,	TM							
US 200	US 20080318915 A1 20081225 US 2007-765657 20070620															
PRIORITY A	PRIORITY APPLN. INFO.: US 2007-765657 A 20070620															
ASSIGNMENT	ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT															
OTHER SOURCE(S): MARPAT 150:64039																

OTHE AB The present application describes deuterium-enriched fluticasone

propionate, pharmaceutically acceptable salt forms thereof, and methods of treating using the same. In the examples, four deuterium-enriched fluticasone propionate compds. are presented, and a synthesis scheme is

provided.

80474-14-2DP, Fluticasone propionate, deuterium-enriched RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(deuterium-enriched fluticasone propionate for treating asthma, allergic rhinitis, eczema, and psoriasis)

80474-14-2 CAPLUS RN

Androsta-1, 4-diene-17-carbothioic acid, CN

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA

INDEX NAME)

3

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:237775 CAPLUS

DOCUMENT NUMBER: 148:355999

TITLE: Method for preparing fluticasone propionate

INVENTOR(S): Shen, Yuliang; Liu Xirong; Xie, Laibin; He, Huixian PATENT ASSIGNEE(S): Steroid Chemicals Co., Ltd., Peop. Rep. China SCOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, Ilpo.

CODEN: CNXXEV
DOCUMENT TYPE: Patent

LANGUAGE: Chinese FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	API	PLICATION NO.	DATE
CN 101125875	A	20080220	CN	2007-10044880	20070815
CN 100549022	C	20091014			
PRIORITY APPLN. INFO.:			CN	2007-10044880	20070815

OTHER SOURCE(S): CASREACT 148:355999

GI

AB Fluticasone propionate is prepared by (1) allowing to react compound $1(6\alpha, 9\alpha-difluoro-11\beta-hydroxy-16\alpha-methyl-17\alpha-$

propionyloxy-3-one-androst-1,4-diene-17B-thiocarboxylate) with XCH2Br (X = Cl, Br, iodo) at a molar ration of 1-5:1 in solvent in the presence of alkali at 0-150°C for 0.2-5 h to obtain halide I; (2) then reacting with ammonium tetraalkyl fluoride or M+F= in the presence of ion solution and solvent at $20\text{-}100^\circ\text{C}$ for 0.1-24 h to obtain the product with formula 3, wherein M+F= is fluoride of alkaline metal ion, alkaline earth metal ion or transition metal ion, alkali is hydroxide, phosphate or $\frac{1}{2}$ fluoride $\frac{1}{2}$ fluoride fluor

carbonate of alkaline metal or alkaline earth metal, or organic base. Ion solution is

[Bmim][X], wherein [Bmim] is 1-butyl-3-methylimidazole; [X] is BF4, PF6, SbF6, OTf or NTF2. Solvent used in step (1) is DMSO, N,N-DMF, acetone, methanol, ethanol, acetonitrile, dichloromethane, petroleum ether, toluene and/or xylene; solvent used in step (2) is DMSO, N,N-DMF, acetoner, ethanol, acetonitrile, 1,4-dioxane, tert-butanol, dichloromethane, petroleum ether, toluene and/or xylene. Tetraalkylammonium fluoride is Cl-C2O tetraammonium fluoride with or without crystal water. The molar ratio of tetraalkylammonium fluoride to I, M+F- to I and ion solution to I is 1-5:1, 1-6:1 and 0.1-6:1 resp. The method has advantages of simple operation process, high yield, low cost, convenience for post treatment

and promising industrial prospect.

IT 80474-14-2P, Fluticasone propionate RI: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of fluticasone propionate)

RN 80474-14-2 CAPLUS

CN Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, (6a,11B,16a,17a)- (CA

INDEX NAME)
Absolute stereochemistry.

IT 80474-45-9

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of fluticasone propionate)

RN 80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, $(6\alpha,11\beta,16\alpha,17\alpha)$ - (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L38 ANSWER 8 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:1454878 CAPLUS

DOCUMENT NUMBER: 148:55252

TITLE: Novel process for the preparation of fluticasone propionate, a therapeutically useful glucocorticoid

anti-inflammatory agent

INVENTOR(S): Gore, Vinavak G.; Gadakar, Mahesh; Pokharkar, K.; Wakchure, V.

PATENT ASSIGNEE(S):

Generics UK, Limited, UK; Merck Development Centre Private Limited

SOURCE:

PCT Int. Appl., 41 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

PAT	TENT	NO.			KIN	D	DATE			APPL	ICAT	ION	NO.		D.	ATE	
WO	2007	1446	68				2007 2008				007-				2	0070	611
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BH,	BR,	BW,	BY,	BZ,	CA,
		CH,	CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DO,	DZ,	EC,	EE,	EG,	ES,	FI,
		GB,	GD,	GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,
		KM,	KN,	KP,	KR,	KZ,	LA,	LC,	LK,	LR,	LS,	LT,	LU,	LY,	MA,	MD,	MG,
		MK,	MN,	MW,	MX,	MY,	MZ,	NA,	NG,	NI,	NO,	NZ,	OM,	PG,	PH,	PL,	PT,
		RO,	RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	SV,	SY,	TJ,	TM,	TN,	TR,
		TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	ZA,	ZM,	ZW					
	RW:	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HU,	IE,
		IS,	IT,	LT,	LU,	LV,	MC,	MT,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,	BF,
		ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG,	BW,
		GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,
							TJ,										
AU	2007	2589	49		A1		2007	1221		AU 2	007-	2589	49		2	0070	611
CA	2654	644					2007										
EP	2044	099			A2		2009	0408		EP 2	007-	7337	49		2	0070	611
	R:	ΑT,	BE,	ВG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	ΗU,	ΙE,
		IS,	IT,	LI,	LT,	LU,	LV,	MC,	MT,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,
		AL,	BA,	HR,	MK,	RS											
	2009						2009	0709								0081	
PRIORITY	APP	LN.	INFO	. :						IN 2						0060	
										IN 2						0060	
										WO 2	007-0	GB50	328	1	W 2	0070	611

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): CASREACT 148:55252; MARPAT 148:55252

GI

10/552,118

AB A novel process was disclosed for the preparation of the steroidal 178-carboxylic thioate fluticasome propionate I (R17 = COCH2Me, R20 = CH2F) and comprised the use of soluble mixed fluorides to introduce fluorine by displacing an appropriate leaving group X in compds., such as I (R17 = COCH2Me, R20 = CH2X, X = Cl, Br, iodo, OSO2FH, OSO2C6H4-4Me, OSO2Me, OSO2CFF3, OCOMe), resulting in selective and controlled fluorination without the formation of undesirable byproducts.

IT 80474-14-2P, Fluticasone propionate Rl: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(process for the preparation of fluticasone propionate, a therapeutically useful glucocorticoid anti-inflammatory agent)

RN 80474-14-2 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

Ι

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, (6 α ,11 β ,16 α ,17 α)- (CA INDEX NAME)

Absolute stereochemistry.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L38 ANSWER 9 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:789323 CAPLUS

DOCUMENT NUMBER: 147:257929

TITLE: Method for synthesis of Fluticasone propionate

INVENTOR(S): Qin, Guoru

PATENT ASSIGNEE(S): Gaoyou Zhaokang Pharmaceutical Co., Ltd., Peop. Rep.

China

SOURCE: Faming Zhuanli Shenging Gongkai Shuomingshu, 18pp.

CODEN: CNXXEV
DOCUMENT TYPE: Patent

LANGUAGE: Chinese FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	API	PLICATION NO.	DATE
CN 100999541	A	20070718	CN	2006-10161627	20061219
CN 100497367	C	20090610			
PRIORITY APPLN. INFO.:			CN	2006-10161627	20061219
OTHER SOURCE(S):	CASRE	CT 147:25792	9		

AB The title compound was synthesized from Flumethasone oxidation with sodium

periodate or periodic acid to obtain

 6α , 9α -difluoro- 11β , 17α -dihydroxyl- 16α -methyl-

3-oxy-androstane-1,4-diene-17 β -carboxylic acid; thiolation with

N,N-dimethylthioaminoformyl chloride in the presence of

diisopropylethylamine; and potassium iodide to give

 6α , 9α -difluoro-11 β -hydroxyl-16 α -methyl-3-oxy-

androstane-1,4-diene-17 β -thiocarboxylic acid; esterification with

propanoyl chloride; and sulfur alkylation with bromofluoromethane in the presence of potassium carbonate as catalyst. This invention has the advantages of a short reaction process, high yield, low cost, and high

product purity.

IT 80474-45-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(synthesis of Fluticasone propionate from Flumethasone)

RN 80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-,

 $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 80474-14-2P, Fluticasone propionate
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of Fluticasone propionate from Flumethasone)
RN 80474-14-2 CAPLUS

CN Androsta-1,4-diene-17-carbothioic acid,
6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-,
S-(fluoromethyl) ester, (6x,1)P,16x,17a)- (CA

INDEX NAME)
Absolute stereochemistry.

10/552,118

L38 ANSWER 10 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:771505 CAPLUS

DOCUMENT NUMBER: 148:246376

TITLE: Simple & improved process for the preparation of androstane intermediates useful for preparation of anti-inflammatory compounds

INVENTOR(S): Naravanrao, Kankan Rajendra; Ramachandra, Rao

Dharmarai; Purshottam, Pande Vidvadhar

PATENT ASSIGNEE(S): Cipla Limited, India

Indian Pat. Appl., 18pp. SOURCE:

CODEN: INXXBQ DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PAT	TENT	NO.	KII
IN	2005	MU00438	A

ND DATE APPLICATION NO. DATE 20070706 IN 2005-MU438 20050406 PRIORITY APPLN. INFO .: IN 2005-MU438 20050406 CASREACT 148:246376 OTHER SOURCE(S):

Disclosed herein is a simple, one-pot process for the preparation of fluticasone propionate comprising treating the compound of formula II with piperidine to obtain compound of formula III, which is reacted in situ with bromo fluoro methane in the absence of any inorg, base to yield a compound of formula (I). The invention also discloses process for preparation of compound

of formula III.

80474-14-2P, Fluticasone propionate

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of androstane derivs. use for preparation of anti-inflammatory compds.)

RN 80474-14-2 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA

INDEX NAME)

10/552,118

L38 ANSWER 11 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:321341 CAPLUS

DOCUMENT NUMBER: 146:337279

TITLE: Process for sublimation of nonvolatile organic

compounds by heating on a conducting grid
INVENTOR(S): Komarov, V. S.; Mikhalev, S. P.; Morozov, Yu. N.;

Sergeev, G. B.

PATENT ASSIGNEE(S): 000 "Nanokriokhimiva", Russia

KIND DATE

SOURCE:

Russ., 7pp. CODEN: RUXXE7

DOCUMENT TYPE: Patent

LANGUAGE: Russian FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.

RU	2295511	C1	20070320	RU 2005-141574	20051230
PRIORIT:	APPLN. INFO.:			RU 2005-141574	20051230
				ed by heating them on a	
gr:	id, preferably mad	le of me	etal, through	n which elec. current i	s passed,
suc	ch that a layer of	organ:	ic material i	is deposited on the gri	d and this layer
is	mech. pressed to	the gr:	id. In examp	oles given, thiourea, g	abapentin and
flu	iticasone propiona	te are	purified by	this process of sequen	tial
sul	olimation-condensa	ation wa	ith final pro	duct purities of 99.2-	99.6%. This

APPLICATION NO.

DATE

sublimation-condensation with final product purities of 99.2-99.6%. The process results in accelerated sublimation and increased purity of sublimed product. Drawings of the apparatus used are included.

IT 80474-14-2P, Fluticasone propionate RL: PEP (Physical, engineering or chemical process); PUR (Purification or

recovery); PREP (Preparation); PROC (Process)
(process for sublimation of nonvolatile organic compds. by heating on

conducting grid)

RN 80474-14-2 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA

S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA INDEX NAME)

L38 ANSWER 12 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:113502 CAPLUS

DOCUMENT NUMBER: 146:184636

TITLE: Method for preparation of Fluticasone propionate

INVENTOR(S): Chu, Dingjun; Zhang, Defa

PATENT ASSIGNEE(S): Shanghai Aurisco International Trading Co., Ltd.,

Peop. Rep. China SOURCE: PCT Int. Appl., 14pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

FAMILY ACC. NUM. COUNT: 1

W0 2007012228 A1 20070201 W0 2005-CN1339 W: AE, AG, AL, AH, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CM, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FT, GB, GE, GH, GM, HR, HU, ID, II, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LK, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MZ, AZ, AZM, ZW, ST, TJ, TM, TM, TR, TT, TZ, UA, UG, US, UZ, VC, VN, VX, AZ, ZM, ZW, CM, CG, CG, CG, CG, CG, CG, CG, CG, CG, CG	P.	ATE	TI	NO.			KIN		DATE			APPL	ICAT	ION	NO.		D.	ATE	
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GB, GE, GH, M, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KE, KR, SK, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SE, SE, SE, SE, SE, SE, SE, SE, SE, SE	W	0 20	007	0122	28				2007	0201		WO 2	005-	CN13	39		2	0050	829
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MX, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU ZA, ZM, ZM RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY KG, KZ, MD, RU, TJ, TM CN 1903871 A 20070131 CN 2005-10028147 20050726 EF 1911741 A1 20080416 EP 2005-781841 20050829 EF 2911741 A1 20080416 EP 2005-781841 20050829 EF 15, IT, LI, LI, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR US 20080125407 A1 20080429 US 2008-20519 20080126 IN 2008DN01479 A 20080404 IN 2008-200519 20080126 IN 2008DN01479 A 20080404 IN 2008-20014 A 20050726 SIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT HERE SOURCE(S): CASREACT 146:184636 B A method for preparing S-fluoromethyl-6α, ad-difluoro-11β-hydroxy-16α-methyl-17α-propionyloxy-3-oxo-androsta-1, 4-diene- 17β-Carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. N 80474-45-9 CREPUS		1	₹:																
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MZ, NA NG, NI, NO, NIZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SG, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU ZA, ZM, ZW RN: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, CH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY KG, KZ, MD, RU, TJ, TM CN 1903871 CN 100560598 EF 1911741 Al 20070131 CN 20080125407 Al 20080416 EF 2005-781841 20080125407 Al 20080529 LIT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, ST, TJ, UG, CM, CM, CM, CM, CM, CM, CM, CM, CM, CM				CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, TE IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GR, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AN, AZ, BY CON 100560598 C 20071118 CN 2005-10028147 20050726 EP 1911741 A1 20080416 EP 2005-781841 20050829 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, TE IS, IT, LI, LU, VW, MC, NL, PL, PT, RO, SE, SI, SK, TR US 20080125407 A1 20080426 US 2008-20519 20080126 IN 2008D001479 A 20080429 US 2008-20519 20080126 IN 2008D001479 A 20080404 IN 2008-D01479 A 20050726 SIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT HER SOURCE(S): CASFRACT 146:184636 A method for preparing S-fluoromethyl-GG, 9α-difluoro-11β-hydroxy-16α-methyl-17α-propionyloxy-3-oxo-androsta-1, 4-diene-17β-carbothioate (Pluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. 80474-45-99 RL: RCT (Reactant); SPN (Synthetic preparation); PREF (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) 80474-45-9 CALUS																			
SI, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, RR, BF, BJ CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GR, M, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY KG, KZ, MD, RU, TJ, TM CN 1903871 A 20070131 CN 2005-10028147 20050726 C 20091118 EF 1911741 A 1 20050428 EF 1911741 A 1 20050416 EF 2005-781841 20050829 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE SCHOOL CONTROL																			
ZA, ZM, ZW RN: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, TE IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BT CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY CN 1908671 A 20070131 CN 2005-10028147 20050726 CN 100560598 C 20091118 EP 1911741 A1 20080416 EP 2005-781841 20050829 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE IS, IT, LI, LU, LV, WC, NL, PL, PT, RO, SE, SI, SK, TR US 20080125407 A1 20080529 US 2008-20519 20080126 IN 2008D001479 A 20080404 IN 2008-D01479 20080220 IORITY APPLN. INFO: CN 2005-10028147 A 20050726 SIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT HER SOURCE(S): CASREACT 146:184636 A method for preparing 5-fluoromethyl-6α, 9α-difluoro-11β-hydroxy-16α-methyl-17α-propionyloxy-3-oxo-androsta-1, 4-diene- 17β-carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. 80474-45-9F RL: RCT (Reactant); SPN (Synthetic preparation); PREF (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason)																			
RN: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, RR, BF, BJ CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZW, ZW, AM, AZ, BY KG, KZ, MD, RU, IJ, TM CN 1903871 A 20070131 CN 2005-10028147 20050726 EP 1911741 A 1 20080416 EP 2005-781841 20050829 R 1S, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR US 20080125407 A1 2008042 US 2008-20519 20080125 IN 2008010479 A 20080404 IN 2008-20519 20080220 IN 2008010479 A 20080404 IN 2008-201479 20080220 INTITY APPLN. INFO: CASREACT 146:184636 WG 2005-CN1339 W 20050829 EM 2008CE(S): CASREACT 146:184636 WG 2005-CN1309 CN 20							ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UΖ,	VC,	VN,	YU,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ CF, CG, CI, CM, GA, GM, ML, MR, NE, SN, TD, TG, BW, GM, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY KG, KZ, MD, RU, TJ, TM CN 1903871 A 20070131 CN 2005-10028147 20050726 CN 100560598 C 20091118 EP 2005-781841 20050829 EP 1911741 A 1 20080416 EP 2005-781841 20050829 ER: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE IS, IT, LI, LU, VU, MC, NL, PL, PT, RO, SE, SI, SK, TR US 20080125407 A1 20080529 US 2008-20519 20080126 IN 2008D001479 A 20080529 US 2008-20519 20080126 IN 2008D001479 A 20080529 US 2008-20519 20080126 EN 2005D001479 A 20080529 US 2008-20519 20080126 EN 2005D001479 A 20080529 US 2008-20519 ENGINEENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT HER SOURCE(S): CASREACT 146:184636 A method for preparing S-fluoromethyl-6a, 9a-difluoro-11β-hydroxy-16a-methyl-17a-propionyloxy-3-oxo-androsta-1, 4-diene- 17β-carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. 80474-45-9F ER: RCT (Reactant); SPN (Synthetic preparation); PREF (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason)																			
CF, CG, CI, CM, GA, CN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY KG, KZ, MD, RU, TJ, TM CN 1903871 A 20070131 CN 2005-10028147 20050726 EP 1911741 A 1 20080416 EP 2005-781841 20050829 EP 1911741 A 1 20880416 EP 2005-781841 20050829 EP 15, ST, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE IS, TT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR US 20080125407 A1 20080404 IN 2008-2019 20080126 IN 20080101479 A 20080404 IN 2008-2019 20080220 IORITY APPLN. INFO: WC 2005-10028147 A 20050229 EIGHTY APPLN. INFO: WC 2005-10028147 A 20050229 A 2008CE(S): A SCREACT 146:184636 A method for preparing S-fluoromethyl-6 α , 9 α -difluoro-11 β -hydroxy-16 α -methyl-17 α -propionyloxy-3-oxo-androsta-1, 4-dien-17 β -carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenient1 mild conditions with high product purity, and be suitable for com. pro on a large scale. $80474-45-99$ RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) $80474-45-99$ CALUS		1	RW:																
GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, EY KG, KZ, MD, RU, TJ, TM CN 1903871 CN 20050598 C 20091118 EP 1911741 A1 20080416 EP 2005-781841 CN 200505098 ER: A1, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR US 20080125407 A1 2008029 US 2008-20519 20080126 IN 2008BN01479 A 2008029 US 2008-20519 20080126 IN 2008BN01479 A 2008029 US 2008-20519 20080126 IN 2008BN01479 A 20050726 CN 2005-10028147 A 20050726 SIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT HER SOURCE(S): CASPEACT 146:184636 A method for preparing S-fluoromethyl-6α, 9α-difluoro-11β-hydroxy-16α-methyl-17α-propionyloxy-3-oxo-androsta-1, 4-diene- 17β-carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. 80474-49-9P RL: RCT (Reactant); SPN (Synthetic preparation); PREF (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) 80474-45-9 CAPLUS																			
KG, KZ, MD, RU, TJ, TM CN 1903871 A 20070131 CN 100560598 C 20091118 EP 1911741 A1 20080416 EP 2005-781841 20050829 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR US 20080125407 A1 20080529 IN 2008001479 A 20080404 IN 2008-20519 20080125 IN 2008001479 A 20080404 IN 2008-20519 20080125 IN 2008001479 A 20080404 IN 2005-10028147 A 20050726 KO 2005-201339 W 20050829 SIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISELAF FORMATHER SOURCE(S): A method for preparing S-fluoromethyl-6α, 9α-difluoro-11β-hydroxy-16α-methyl-17α-propionyloxy-3-oxo-androsta-1, 4-dien-17β-carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. 80474-45-9p RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason)																			
CN 1903871 A 20070131 CN 2005-10028147 20050726 CN 100560598 C 20091118 EP 1911741 A1 20080416 EP 2005-781841 20050829 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR US 2000125407 A1 20080529 US 2008-20519 20080126 IN 2008N01479 A 20080529 US 2008-20519 20080126 IN 2008N01479 A 20080529 US 2008-20519 20080126 SIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT HER SOURCE(S): CASREACT 146:184636 A method for preparing S-fluoromethyl-6α, 9α-difluoro-11β-hydroxy-16α-methyl-17α-propionyloxy-3-oxo-androsta-1, 4-diene-17β-carptohioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. 80474-49-59 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) 80474-459- CAPLUS										SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
CN 100560598 C 20091118 EP 1911741 A1 20080416 EP 2005-781841 20050829 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR US 20080125407 A1 20080529 US 2008-20519 20080126 IN 2008001479 A 20080529 US 2008-20519 20080126 IN 2008001479 A 20080529 US 2008-20519 20080226 IORITY APPLN. INFO: CN 2005-10028147 A 20050726 W2005-CN1339 W 20050829 SIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT HER SOURCE(S): CASREACT 146:184636 A method for preparing S-fluoromethyl-6α, 9α-difluoro-11β-hydroxy-16α-methyl-17α-propionyloxy-3-oxo-androsta-1, 4-dien- 17β-carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. 80474-49-59 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason)					KZ,	MD,	RU,	ТJ,	$^{\text{TM}}$										
EP 1911741 A1 20080416 EP 2005-781841 20050829 R: AT, BE, BG, CB, CY, CZ, DB, DK, EE, ES, FI, FR, GB, GR, HU, IE IS, IT, LI, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR US 20080125407 A1 20080529 US 2008-20519 20080220 IN 2008-001479 A 20080404 IN 2008-001479 200801220 IORITY APPLN. INFO.: W0 2005-CN1339 W 20050829 SIGNMENT HISTORY FOR US PATENT AVAILABLE IN LUSD DISPLAY FORMAT HER SOURCE(S): CASKEACT 146:18463 6 A method for preparing S-fluoromethyl-6 α , 9α -difluoro-11 β -hydroxy-16 α -methyl-17 α -propionyloxy-3-oxo-androsta-1, 4-diene-17 β -carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenient1 mild conditions with high product purity, and be suitable for com. pro on a large scale. 80474-45-9P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) 80474 -45-9 CAPLUS							A		2007	0131		CN 2	005-	1002	8147		2	0050	726
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, BU, TE IS, IT, LT, LU, VM, MC, NL, PL, PT, RO, SE, SI, SK, TR US 20080125407 Al 20080259 US 2008-20519 20080126 IN 2008001479 A 20080404 IN 2008-DN1479 20080202 IORITY APPLN. INFO: CN 2005-10028147 A 20050726 W0 2005-CN1339 W 20050829 SIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT HER SOURCE(S): CASREACT 146:184636 A method for preparing S-fluoromethyl- $6a$, $9a$ -difluoro- 11β -hydroxy- $16a$ -methyl- $17a$ -propionyloxy- 3 -oxo-androsta- 1 , 4 -dien- 17β -carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. $80474-45$ -Sp RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) $80474-45$ -9 CAPLUS	C.	N 10	005	60598	В		С		2009	1118									
IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR US 20080125407 Al 20080529 US 2008-20519 20080126 IN 20080129 A 20080404 IN 2008-DN1479 20080126 IORITY APPLN. INFO.: CN 2005-10028147 A 20050726 W0 2005-CN1339 W 20050726 W0 2005-CN1339 W 20050829 SIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT HER SOURCE(5): CASKBACT 146:184636 A method for preparing S-fluoromethyl-6 α , 9α -difluoro-11 β -hydroxy-16 α -methyl-17 α -propionyloxy-3-oxo-androsta-1, 4-diene-17 θ -carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. $80474-45$ -9P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) $80474-45$ -9 CAPLUS	E																		
US 20080125407 Al 20080259 US 2008-20519 20080126 IN 20080001479 A 20080404 IN 2008-0001479 A 20080205 IN 2008001479 A 20080205 IN 2008001479 A 20050726 UN 2005-10028147 A 20050726 UN 2005-000339 W 2005-000339 W 2005-000339 W 20050829 HER SOURCE(S): CASREACT 146:184636 A method for preparing S-fluoromethyl-6 α , 9α -difluoro- 11β -hydroxy- 16α -methyl- 17α -propionyloxy- 3 -oxo-androsta- 1 -diene- 17β -carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. $80474-49-59$ RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) $80474-45-9$ CAPLUS		I	₹:																ΙE,
IORITY APPLN. INFO.: CM 2005-10028147 A 20050726 SIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT HERS SOURCE(S): CASREACT 146:184636 A method for preparing 5-fluoromethyl-6α, 9α-diffluoro-11β- hydroxy-16α-methyl-17α-propionyloxy-3-oxo-androsta-1,4-diene- 17β-carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. 80474-45-9F RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) 80474-45-9 CAPLUS																			
IORLITY APPLM. INFO.: CM 2005-10028147 A 20050726 SIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT HER SOURCE(S): CASREACT 146:184636 A method for preparing 5-fluoromethyl-6α, 9α-diffluoro-11β- hydroxy-16α-methyl-17α-propionyloxy-3-oxo-androsta-1,4-diene- 17β-carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. 80474-45-9F RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) 80474-45-9 CAPLUS	U	S 20	008	0125	407		A1		2008	0529		US 2	008-	2051	9		2	0080	126
SIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT HER SOURCE(S): CASREACT 146:184636 A method for preparing S-fluoromethyl-6a,9a-difluoro-11B-hydroxy-16a-methyl-17a-propionyloxy-3-0xo-androsta-1,4-diene-17B-carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. 80474-45-9P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) 80474-45-9 CAPLUS	I.	N 20	008	DN01	479		A		2008	0404		IN 2	-800	DN14	79		. 2	0800	220
SIGMMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT HER SOURCE(S): CASERACT 146:184636 A method for preparing S-fluoromethyl-fa, 9\(\alpha\)-diffluoro-11\(\beta\)-hydroxy-16\(\alpha\)-methyl-17\(\alpha\)-propionyloxy-3-oxo-androsta-1,4-diene-17\(\beta\)-carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. 80474-45-9P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) 80474-45-9 CAPLUS	TORT	TY	APP	LN	TNEO	. :						CN 2	005-	1002	814/		A Z	0050	/26
<pre>HER SOURCE(S): CASREACT 146:184636 A method for preparing S-fluoromethyl-6α,9α-difluoro-11β-hydroxy-16α-methyl-17α-propionyloxy-3-oxo-androsta-1,4-diene- 17β-carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. 80474-45-9P RL: RCT (Reactant); SPN (Synthetic preparation); PREF (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) 80474-45-9 CAPLUS</pre>																		0050	829
A method for preparing S-fluoromethyl-6a,9a-difluoro-11B-hydroxy-16a-methyl-17a-propionyloxy-3-oxo-androsta-1,4-diene- 17B-carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. 80474-45-99 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) 80474-45-9 CAPLUS													US D	ISPL	AY F	JRMA	T		
hydroxy-16u-methyl-17u-propionyloxy-3-oxo-androsta-1, 4-diene- 17β-carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. 80474-45-99 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) 80474-45-9 CAPLUS													-116		- 11				
17B-carbothioate (Fluticasone propionate) from Flumethason was disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. 80474-45-59 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) 80474-45-9 CAPLUS																			
disclosed. The claimed method can be conducted simply and convenientl mild conditions with high product purity, and be suitable for com. pro on a large scale. 80474-45-9P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) 80474-45-9 CAPLUS																			
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on a large scale. 80474-45-99 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) 80474-45-9 CAPLUS																			
80474-45-99 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); R (Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) 80474-45-9 CAPLUS							11 1114	an F	Loui	ct p	ULIU	у, а	iiu b	e su	ıtab.	re r	OI C	JIII	proc
RL: RCT (Reactant); SPN (Synthetic preparation); R(Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) 80474-45-9 CAPLUS					scar	٠.													
(Reactant or reagent) (preparation of Fluticasone propionate from Flumethason) 80474-45-9 CAPUUS					act a	o+ \ .	CDM	10.	nt ho	+10.	oror	arat	ionl	. DD	FD /	Dron	arat	ioni	. D7
(preparation of Fluticasone propionate from Flumethason) 80474-45-9 CAPLUS								(5)	nune	CIC 1	prer	arat	1011)	,	DE (rep	arac	LOII)	, 100
80474-45-9 CAPLUS								icas	one i	nron	iona	te f	rom	Flum	et ha	son)			
							L LUL.		Jone	Prop.	-0116	ce I	LOIN	- 10111	- ciidi	JJ11)			
	я																		
6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-,	A	ndr	st	a-1,	4-di	ene-							(1-0	xopr	xogo	v)			

Absolute stereochemistry. Rotation (-).

RN 80474-14-2 CAPLUS CN Androsta-1,4-diene-17-carbothioic acid,

Androsca-1, a-defect for arbothors acid, 6,9-diffuor-oll-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, $(6\alpha,11\beta,16\alpha,17\alpha)$ - (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L38 ANSWER 13 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2006:381179 CAPLUS

DOCUMENT NUMBER: 144:412741

TITLE: Process for preparation of fluticasone analogs via

esterification of a carbothioic acid

INVENTOR(S): Sobral, Luis; Martin, Dionisio; Heggie, William;

Leitaeo, Emilia

PATENT ASSIGNEE(S): Hovione Inter Ltd., Switz.; Turner, Craig Robert

SOURCE: PCT Int. Appl., 18 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

		ENT I						DATE				LICAT					ATE	
												2004-					0041	202
		W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB	, BG,	BR,	BW,	BY,	BZ,	CA,	CH,
			CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ	, EC,	EE,	EG,	ES,	FI,	GB,	GD,
			GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS	, JP,	KE,	KG,	KP,	KR,	KZ,	LC,
			LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG	, MK,	MN,	MW,	MX,	MZ,	NA,	NI,
			NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU	, SC,	SD,	SE,	SG,	SK,	SL,	SY,
			TJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US	, UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW
		RW:	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE	, ES,	FI,	FR,	GB,	GR,	HU,	IE,
			IS,	IT,	LT,	LU,	MC,	NL,	PL,	PT,	RO	, SE,	SI,	SK,	TR,	BF,	ВJ,	CF,
			CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR	, NE,	SN,	TD,	TG,	BW,	GH,	GM,
			KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ	, UG,	ZM,	ZW,	AM,	AZ,	BY,	KG,
			KZ,	MD,	RU,	TJ,	TM											
I	ΑU	2004	3242	37		A1		2006	0427		AU	2004-	3242	37		2	0041	202
(CA	2584	052			A1		2006	0427		CA	2004-	2584	052		2	0041	202
E	ΞP	1802	647			A1		2007	0704		EP	2004-	8223	30		2	0041	202
		R:	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE	, ES,	FI,	FR,	GB,	GR,	HU,	IE,
			IS,	IT,	LI,	LT,	LU,	MC,	NL,	PL,	PT	, RO,	SE,	SI,	SK,	TR		
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Ţ	JS	2007	0287	846		A1		2007	1213		US	2007-	5774	62			0070	
PRIOR	IΤ	APP:	LN.	INFO	. :							2004-					0041	
											WO	2004-	GB50	52		W 2	0041	202

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 144:412741

AB A process for preparing esters, such as I (R = CO(CH2)n, COCHMe2, n = 1, 2), was disclosed and comprised esterification of the C-17 hydroxyl group of 6α , 9α -difluoro- 11β , 17α -dihydroxy- 16α -methyl-3-oxoandrosta-1, 4-diene- 17β -carbothioic acid I (R = H) with a slight excess of a corresponding acyl chloride, RCOCl, in an inert solvent in the presence of a tertiary amine.

80474-14-2P, Fluticasone propionate 80474-45-9P RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(process for preparation of pharmaceutically useful fluticasone analogs via esterification of a corresponding carbothioic acid)

RN 80474-14-2 CAPLUS CN Androsta-1,4-diene-3

Androsta-1,4-diene-17-carbothioic acid, 6,9-diffuoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, (6a,11β,16a,17a)- (CA INDEX NAME)

Ι

Absolute stereochemistry.

RN 80474-45-9 CAPLUS

CN Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6a,118,16a,17a)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

REFERENCE COUNT:

4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L38 ANSWER 14 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2006:74597 CAPLUS

DOCUMENT NUMBER: 144:156707

TITLE: Novel crystalline forms of 6α , 9α -difluoro- 11β -hydroxy- 16α -

methyl-3-oxo-17 α -propionyloxy-androsta-1,4-diene 17 β -carboxylic acid and processes for preparation

INVENTOR(S): Adin, Itai; Iustain, Carmen; Futerman, Yuri

PATENT ASSIGNEE(S): Adin, Ital; Iustain, Carmen; Futern
Chemagis Ltd., Israel

SOURCE: U.S. Pat. Appl. Publ., 46 pp.

CODEN: USXXCO
DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA	TENT	NO.			KIN	D	DATE			APPL	ICAT	ION	NO.		D.	ATE	
	2006 2575		937		A1 A1		2006 2006			US 2 CA 2						0050	
WO	2006	0111	48		A2		2006	0202		WO 2	005-	IL80:	2		2	0050	726
WO	2006	0111	48		A3		2009	0108									
	W:	CN,	co,	CR,	CU,	CZ,	DE,	DK,	DM,	BB, DZ, IS,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
		LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,
		SL,		SY,						TZ,							
	RW:	AT,	BE,	BG,						EE,							
		GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	ML, SZ,	TZ,						
	2433	258			RU,					EP, GB 2	007-					0050	
PRIORIT	Y APP	LN.	INFO	. :						US 2 US 2	004-	5998	75P	1	P 2	0040 0040	810
										US 2 WO 2						0040 0050	

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT AB Novel crystalline forms II, III, IV, V, VI, VII and VIII of

 6α , 9α -difluoro-11 β -hydroxy-16 α -methyl-3-oxo-

 17α -propionyloxyandrosta-1,4-diene- 17β -carboxylic acid, a chemical intermediate useful in the preparation of fluticasone propionate, and novel methods of making these forms, substantially free of water, are disclosed.

IT 80474-45-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(crystalline forms of 6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-propionyloxy-androsta-1,4-diene

 $17\beta\text{-carboxylic}$ acid for prpg. fluticasone propionate)

RN 80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA INDEX NAME)

(ou, 11p, 1ou, 1/u) - (CA INDEA NAME

Absolute stereochemistry. Rotation (-).

IT 80474-14-2P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (crystalline forms of 6α , 9α -difluoro-11 β -hydroxy-16 α -

methyl-3-oxo-17α-propionyloxy-androsta-1,4-diene

- 17β -carboxylic acid for prpg. fluticasone propionate)
- RN 80474-14-2 CAPLUS
- CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, $(6\alpha,11\beta,16\alpha,17\alpha)$ - (CA INDEX NAME)

Absolute stereochemistry.

L38 ANSWER 15 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2006:36999 CAPLUS

DOCUMENT NUMBER: 144:108501

TITLE: Synthesis and powder preparation of fluticasone

propionate

INVENTOR(S): Kaspi, Joseph; Arad, Oded; Brand, Michael; Shookrun,

Moty; Malka, Simona; Alnabari, Mohammed; Hazan,

Shalom; Malesevic, Vlado

PATENT ASSIGNEE(S): Israel

U.S. Pat. Appl. Publ., 27 pp. SOURCE:

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060009435	A1	20060112	US 2005-159241	20050623
PRIORITY APPLN. INFO.:			US 2004-581702P P	20040623
			US 2004-623877P P	20041102

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): CASREACT 144:108501

Fluticasone propionate is prepared from the thiocarboxylic acid precursor and a halofluoromethane in the presence of water and a base in an organic solvent. The prepared fluticasone propionate is spray dried to form a powder that is highly suitable for administration by inhalation. A process of purifying a key intermediate in the synthesis of fluticasone propionate is also disclosed.

80474-14-2P, Fluticasone propionate

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis and powder preparation of fluticasone propionate) 80474-14-2 CAPLUS

RN

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA

INDEX NAME)

Absolute stereochemistry.

IT 80474-45-9

RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and powder preparation of fluticasone propionate)

RN 80474-45-9 CAPLUS

CN Androsta-1,4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6a,11B,16a,17a)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L38 ANSWER 16 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:1028074 CAPLUS

DOCUMENT NUMBER: 143:312038

TITLE: Pharmaceutical formulation comprising an androstane derivative and a solubilizing agent in an aqueous

liquid carrier

INVENTOR(S): Biggadike, Keith; Buxton, Ian; Daley-Yates, Peter Terence; Fong, Bettina; Ho, Elita Y.; Reed, Kenton

Lewis; Sayani, Amyn

PATENT ASSIGNEE(S):

SOURCE: U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of U.S. Ser. No. 66,951.

CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC NUM COUNT: 11

FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PA:	ENT :						DATE									ATE	
	2005										005-						
	2003		676		A1		2003			US 2	002-	6695	1		2	0020	204
	6787				B2		2004										
WO	2003				A1		2003				003-						
	W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW.	MX,	MZ,	NO.	NZ,	OM,	PH.
		PL.	PT.	RO.	RU.	SC.	SD,	SE.	SG.	SK.	SL.	TJ.	TM.	TN.	TR.	TT.	TZ
		UA.	UG.	US.	UZ.	VC.	VN.	YU.	ZA.	ZM.	ZW						
	RW:						MZ,					UG.	7M.	2W.	AM.	A7.	BY
							TM.										
							IE,										
							GA,										
MO	2003						2003								2		204
	W:						AU,										
							DK,										
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							VN,										
	RW:						MZ,										
							TM,										
							ΙE,										BF,
							GA,										
	2003		55		A1 A1		2003	0902		AU 2	003-	2058	55		2	0030	204
	1471	895			A1		2004			EP 2	003-	7027	32		2	0030	204
EΡ	1471				В1		2008										
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT
							RO,										
JΡ	2005	5232	68		T		2005	0804		JP 2	003-	5654	57		2	0030	204
ΕP	1757	281			A2		2007	0228		EP 2	006-	1240	55		2	0030	204
EΡ	1757	281			A3		2009	0715									
	R:	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE
		IT.	LI.	LU.	MC.	NL.	PT.	SE.	SI.	SK.	TR.	LT.	LV.	RO			
ΑT	3967														2	0030	204
	2305				T3		2008 2008	1101			003-				2		
					1.0										-		

W0 2001-058495 A2 20011002 US 2002-66961 A 20020204 EP 2003-702732 A3 20030204 W0 2003-GB485 W 20030204	US 20050175545 PRIORITY APPLN. INFO.:	Al	20050811	US 2 WO 2 GB 2 WO 2 US 2 US 2 EP 2	002-66961 003-702732	W A A1 A2 A A3	20020204 20030204
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OTHER SOURCE(S):

MARPAT 143:312038

AB A pharmaceutical formulation comprising an aqueous carrier liquid having dissolved therein (a) a glucocorticoid and (b) a solubilizing agent for assisting the solubilization of the medicament in the aqueous carrier liquid is described. A solubilizing agent is selected from a surfactant, such as Triton X100 and Tyloxapol. The formulation further comprises a hydroxy-containing organic cosolvating agent, e.g., dextrose, or phosphatidylcholine. For example, a formulation for intranasal delivery was prepared containing fluticasone propionate 0.05%, Triton X-100 5%, dextrose cosolvating agent 4%, BKC 0.015%, BDTA 0.15%, and water to 100%. The formulation, suitable for 120 actuations, was filled into a bottle fitted with a metering valve adapted to dispense 50 or 100 µl per actuation and the device was fitted into a nasal actuator.

IT 80474-14-2P, Fluticasone propionate

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(nasal spray formulation comprising androstane derivative and solubilizing agent in aqueous liquid carrier)

RN 80474-14-2 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, $(6\alpha,11\beta,16\alpha,17\alpha)$ - (CA INDEX NAME)

·

Absolute stereochemistry.

10/552,118

L38 ANSWER 17 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:361853 CAPLUS

DOCUMENT NUMBER: 142:411529

TITLE: A process for preparing androstane 17β-carboxylic

acids and androstane 17B-carbothioic acid

fluoromethyl esters

Vetturini, Emanuela; Farnesi, Sara INVENTOR(S): PATENT ASSIGNEE(S): S.N.I.F.F. Italia S.p.A., Italy

SOURCE: Eur. Pat. Appl., 20 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIN	D DATE	APPL:	ICATION NO.	DATE
EP 1526139	A1	200504	127 EP 20	003-24329	20031024
					NL, SE, MC, PT,
IE,	SI, LT, LV,	FI, RO, N	MK, CY, AL,	TR, BG, CZ,	EE, HU, SK
US 200500906	75 A1	200504	128 US 20	004-969241	20041021
PRIORITY APPLN. I	NFO.:		EP 20	003-24329	A 20031024
ASSIGNMENT HISTOR	Y FOR US PA	TENT AVAIL	LABLE IN LS	US DISPLAY FO	ORMAT
OTHER SOURCE(S):	CAS	REACT 142:	:411529; MAI	RPAT 142:411	529
GT					

- AB The present invention relates to an oxidation process for preparing androstane 17β -carboxylic acid derivs., such as I [R1, R2 = H, OH; R1R2 = O; X, Y = C1, F; R3 = α -Me, β -Me; R4 = OH, alkanoyloxy; R5 = OH], with a high purity degree by oxidative demolition of the carbon atom 21 of the compound II [R5 = CH2OH] by using hydrogen peroxide in a basic environment in a polar solvent optionally in the presence of water. The invention also discloses a process for preparing fluticasone propionate II [R = CH2F] from androstane-17 β -carbothioic acid derivative II [R = H] and bromofluoromethane.
- 80474-14-2P, Fluticasone propionate

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of androstane 17β-carboxylic acids and androstane 17β-carbothioic acid fluoromethyl esters)

RN 80474-14-2 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, (6α , 11β , 16α , 17α)- (CA INDEX NAME)

Absolute stereochemistry.

IT 80474-45-9

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of androstane 17β-carboxylic acids and androstane 17β-carbothioic acid fluoromethyl esters)

RN 80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

7

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, $(6\alpha,11\beta,16\alpha,17\alpha)$ - (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

REFERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 18 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:857616 CAPLUS

DOCUMENT NUMBER: 141:332364

TITLE: Process for the preparation of steroidal carbothioic

acid derivatives and intermediates

INVENTOR(S): Loevli, Trond; Nygaard, Anne-mette; Reitstoen, Bjoern;

Fivelstad, Magny PATENT ASSIGNEE(S): Alpharma Aps. Den.

SOURCE: PCT Int. Appl., 40 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION:

	rent																	
	2004																	
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,	
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
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		NO,	ΝZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	
		ΤJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW	
	RW:	BW,	GH,	GM,	KΕ,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	
							TJ,											
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				BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	
		TD,																
EP	1466																	
	R:						ES,										PT,	
							RO,											
	2004									AU 2	004-	2263	18		2	0040	402	
	2004																	
	2530																	
EP	1611																	
	R:						ES,											
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	2005															0051		
US	2007						2007	1122										
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										WO 2								
										WU Z	004-	DKZ4	_		w Z	0040	402	

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT CASREACT 141:332364; MARPAT 141:332364 OTHER SOURCE(S):

17β-carboxylic acid, prepared from flumetasone, in DMA was treated with EDC (1-ethyl-3-(3-dimethylaminopropyl)carbodimide) and NHS

(N-hydroxysuccinimide) followed by sodium hydrosulfide hydrate and then bromofluoromethane to give 92% S-fluoromethyl

6α,9α-difluoro-11β-hydroxy-16α-methy1-3-oxo-

AB Steroidal carboxthioc acids were prepared by reacting steroidal carboxylic acids or salts with a coupling agent alone or in conjunction with a coupling enhancer followed by reaction with a nucleophilic agent comprising a sulfur atom. Thus, 6α , 9α -difluoro- 11β -hydroxy- 16α -methyl-3-oxo- 17α -propionyloxyandrosta-1,, 4-diene-

10/552,118

 $17\alpha\text{-propionyloxyandrosta-1,4-diene-17}\beta\text{-carbothioate}$ (fluticasone propionate).

TT 73205-13-7P 80474-14-2P, Fluticasone propionate

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for preparation of steroidal carbothioic acid derivs. and intermediates)

RN 73205-13-7 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-methyl ester, (6 α ,11 β ,16 α ,17 α)- (CA INDEX NAME)

Absolute stereochemistry.

RN 80474-14-2 CAPLUS

Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, $(6\alpha,11\beta,16\alpha,17\alpha)$ - (CA INDEX NAME)

Absolute stereochemistry.

RN 80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6a,11\(\beta\),16a,17a)- (CA INDEX NAME) Absolute stereochemistry. Rotation (-).

14

REFERENCE COUNT:

THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:837305 CAPLUS

DOCUMENT NUMBER: 141:332363

TITLE: Process for the preparation of steroidal

17β-carbothioates INVENTOR(S):

Loevli, Trond; Nygard, Anne Mette; Reitstoen, Bjoern;

Fivelstad, Magny PATENT ASSIGNEE(S): Alpharma Aps. Den.

Eur. Pat. Appl., 18 pp. SOURCE:

CODEN: EPXXDW DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION:

	ATENT												NO.			ATE		
	1466															0030	404	
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
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At	J 2004	2263	18		A1		2004	1014		AU 2	004-	2263	18		2	0040	402	
At	J 2004	2263	18		B2		2008	0605										
	A 2530									CA 2	004-	2530	680		2	0040	402	
WO	2004	0877	31		A1		2004	1014		WO 2	004-	DK24	2		2	0040	402	
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,	
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
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		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,	
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	
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		ES,	FI,	FR,	GB,	GR,	HU,	IE,	IT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	
		SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	
		TD,	TG															
E	2 1611	149			A1		2006	0104		EP 2	004-	7253	01		2	0040	402	
		AT,																
		IE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	PL,	SK,	HR
Cì	N 1798	757			A		2006	0705		CN 2	004-	8001	5412		2	0040	402	
JE	2006	5220	28		T		2006	0928		JP 2	006-	5043	47		2	0040	402	
NO	2005	0046	36		A		2005	1227		NO 2	005-	4636			2	0051	010	
11	1 2005	CN02	890		A		2007	0406		IN 2	005-	CN28	90		2	0051	103	
US	3 2007	0270	584		A1		2007	1122		US 2	007-	5521	18		2	0070	413	
PRIORIT																		
										DK 2	004-	449			A 2	0040	319	
										WO 2	004-	DK24	2		7 2	0040	402	

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): MARPAT 141:332363

GI

- AB A novel method was disclosed for the conversion of steroidal 17 β -carboxylic acids I (Z = OH) to the corresponding carbothioates I [R1 = H, OH, acyloxy; R2 = H, α -OH, α -, β -alkyl; R1R2 = fused 1,3-dioxolane ring of the form -OCRYR8O-; R3 = OH, protected hydroxyl; R4 = H, halogen; R3R4 = bond, -O- (epoxide); R5 = H, halogen; R7, R8 = H, alkyl; Z = SCH2F, SCH2Fr, S(CH2)2F] including fluticasone propionate II (R1 = COCH2Me, Z = SCH2F), via novel in situ generated 17 β -carboxy imidazolyl- or succinimidyl esters. Thus, flumetasone II (R1 = OH, Z = CH2OH) was oxidized using periodic acid to form the corresponding acid II (R1 = Z = OH) in 98 yield. The the acid was esterified with MeCH2COC1 using NEt3 to give 17 α -propionate II (R1 = OCCCH2Me, Z = OH) in 998 yield, and subsequent treatment of the 17 α -propionate with NHS and FCH2Br gave fluticasone propionate in 75% yield.
- IT 73205-13-7P 80474-14-2P, Fluticasone propionate 80474-45-9P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (process for the preparation of steroidal 17β -carbothioates)

RN 73205-13-7 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-methyl ester, (6a,11\beta,17a)- (CA INDEX NAME)

Absolute stereochemistry.

RN 80474-14-2 CAPLUS

CN Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, (6a,11β,16a,17a)- (CA INDEX NAME)

Absolute stereochemistry.

RN 80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid, 6,9-diffluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6a,11B,16a,17a)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

REFERENCE COUNT:

3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L38 ANSWER 20 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:515530 CAPLUS

DOCUMENT NUMBER: 141:54528

TITLE: Preparation of 17β -fluorinated-androstane esters from androstane 17β -carbothioate intermediates

INVENTOR(S): Da Col, Marco; Cainelli, Gianfranco; Umani Ronchi,

Achille; Sandri, Sergio; Contento, Michele; Fortunato, Giuseppe

PATENT ASSIGNEE(S): Farmabios S.R.L., Italy; Boriani, Maria Adele

SOURCE: PCT Int. Appl., 50 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PAT	TENT	NO.			KIN	D	DATE			APPI	ICAT	ION	NO.		D	ATE		
WO	2004	0529	12		A1		2004	0624		WO 2	2003-1	EP13	908		2	0031	208	
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,	
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	GE,	
		GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KΡ,	KR,	ΚZ,	LC,	LK,	
		LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NI,	NO,	NZ,	
		OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	TJ,	TM,	
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		BY,	KG,	KZ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	
		ES,	FI,	FR,	GB,	GR,	HU,	IE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	
		TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG
CA	2510	609			A1		2004	0624		CA 2	2003-	2510	609		2	0031	208	
AU	2003	2938	03		A1		2004	0630		AU 2	2003-	2938	03		2	0031	208	
EP	1575	983			A1		2005	0921		EP 2	2003-	7891	76		2	0031	208	
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
		IE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	SK		
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MX	2005	0061	06		A		2005	1214		MX 2	2005-	6106			2	0050	608	
US	2006	0116	359		A1		2006	0601		US 2	2005-	5380	83		2	0050	608	
IN	2005	CN01	524		A		2007	0622		IN 2	2005-0	CN15	24		2	0050	705	
RITY	APP	LN.	INFO	. :						IT 2	2002-1	MI26	06		A 2	0021	209	

WO 2003-EP13908

ΙI

W 20031208

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): CASREACT 141:54528; MARPAT 141:54528

Page 98

The present invention discloses a process for the preparation of AR androstane-17 β -carbothioate intermediates, such as I [R = H, COR1; R1 = alkyl; R2 = H, alkyl; OR and R2 = 16a, 17a-isopropylidenedioxy, 16α , 17α -alkylidenedioxy; R4 = SCH(R3)OH; R3 = H, alkyl, (un) substituted Ph, aralkyl; X, Y and Z, in α or β position = H, OH, Cl, F, CO; X,Y = epoxy; dashed line = single or double bond], for their use in preparing 17β -fluorinated-androstane ester derivs, I (R4 = SCH(R3)F). Thus, androst-1,4-diene derivative II (R = COEt, R4 = OH), obtained by the reaction of II (R = H, R4 = OH) and propionyl chloride, was reacted with dimethylthiocarbamoyl chloride to provide dimethylthiocarbamoyl derivative II [R = COEt, R4 = SCONMe2 (III)]. Dimethylthiocarbamoyl derivative III, on treatment with phosphoric acid, provided carbothioic acid derivative II (R = COEt, R4 = SH), which upon reaction with formaldehyde and followed via selective nucleophilic fluorination, afforded 17β-fluorinated-androstane ester derivative II (R = COEt, R4 = SCH2F).

T 80474-45-9P

RL: IMF (Industrial manufacture); RCT (Reactant); SPM (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of 1/B-fluorinated-androstane esters from androstane 17B-carbothioate intermediates)

RN 80474-45-9 CAPLUS

Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6a,11\(\beta\),16a,17\(\alpha\))- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 80474-14-2P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of $17\beta\text{-fluorinated-androstane}$ esters from androstane $17\beta\text{-carbothioate}$ intermediates)

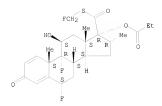
RN 80474-14-2 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA

INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L38 ANSWER 21 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:490444 CAPLUS

DOCUMENT NUMBER: 141:42892

TITLE: Thiocarboxylic acid organic salts and processes

utilizing the same

INVENTOR(S): Brand, Michael; Saeed, Shadi; Davidi, Guy; Arad, Oded

PATENT ASSIGNEE(S): Chemagis Ltd., Israel

SOURCE: U.S. Pat. Appl. Publ., 7 pp.

CODEN: USXXCO DOCUMENT TYPE: Patent

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

PATI	ENT :	NO.			KIN	D	DATE			APP	LICAT	ION	NO.		Dž	ATE	
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US :	2004	0116	396		A1		2004	0617		US	2003-	4063	10		20	0030	404
EP :	1431	305			A1		2004	0623		EP	2003-	2578	79		20	0031	216
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	, IT,	LI,	LU,	NL,	SE,	MC,	PT,
		IE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL	, TR,	BG,	CZ,	EE,	HU,	SK	
ORITY	APP	LN.	INFO	. :						ΙL	2002-	1534	62		A 20	0021	216

PRIORITY APPLN. INFO.: IL 2002-153462 A 200.
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 141:42892

AB The invention provides a thiocarboxylic acid organic amine salts selected from the group consisting of 6,9-difluoro-11-hydroxy-7-propionyloxy-

16α-methylpregna-3-oxo-1,4-diene-17-thiocarboxylic acid

disopropylethylamine salt, triethylamine salt and N-methylpiperidine salt. Fluticasone propionate of high purity is produced according to the following steps: (1) preparing a mixture of the above salts in acetonitrile;

(2) adding to this mixture about a two-fold molar excess of

chlorofluoromethane; (3) heating the mixture at 50° for a specified

period of time; (4) cooling the reaction mixture to a temperature lower than 10°; and (5) separating the precipitated crystals by filtration.

80474-45-9

RN

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of fluticasone propionate with high purity from thiocarboxylic acid organic salts)

80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-,

 $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 80474-14-2P, Fluticasone propionate

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of fluticasone propionate with high purity from thiocarboxylic acid organic salts)

RN 80474-14-2 CAPLUS

CN Androsta-1,4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA

INDEX NAME)

Absolute stereochemistry.

L38 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:41162 CAPLUS

DOCUMENT NUMBER: 140:94192

TITLE: Method for the preparation and isolation of

 6α , 9α -difluoro- 11β , 17α -

dihydroxy-16α-methylpregna-3-oxo-1,4-diene-

17β-carboxylic acid

INVENTOR(S): Rubinsztain, Yaacov; Segal, Ariana; Kaspi, Joseph;

Lerman, Ori

PATENT ASSIGNEE(S): Chemagis Ltd., Israel

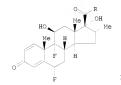
SOURCE: U.S. Pat. Appl. Publ., 4 pp.

CODEN: USXXCO DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040010155	A1	20040115	US 2003-406445	20030404
US 6747163 IL 150654	B2 A	20040608 20061210	IL 2002-150654	20020709
PRIORITY APPLN. INFO.: ASSIGNMENT HISTORY FOR	US PATEN	IT AVAILABLE	IL 2002-150654 IN LSUS DISPLAY FO	A 20020709 RMAT
OTHER SOURCE(S): GI	CASREA	CT 140:9419	2	



AB The invention provides a process for the preparation and isolation of $6\alpha,9\alpha\text{-difluoro-}11\beta,17\alpha\text{-dihydroxy-}16\alpha\text{-}$

methylpregna-3-oxo-1,4-diene-17 β -carboxylic acid [I, R = OH (II)] from flumethasone I [R = CH2OH (III)]. The process involves: (a) oxidation of III in a tetrahydrofuran-water mixture with periodic acid at a temperature lower than 30° C.; (b) cooling the reaction mixture to a temperature lower than 10° C.; (c) adding an antisolvent precooled to a temperature lower than 10° C.; and (d) separating the precipitated crystal od II by filtration. Thus, II is obtained in a yield of at least 98% and of a chromatog, purity of at least 99%.

II 80474-14-2P, Fluticasone-17-propionate RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (preparation of 6α,9α-difluoro-11β,17α-dihydroxy-16α-methylpregna-3-oxo-1,4-diene-17β-carboxylic acid from flumethasone)

RN 80474-14-2 CAPLUS

Androsta-1, 4-diene-17-carbothioic acid, CN 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L38 ANSWER 23 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:3108 CAPLUS

DOCUMENT NUMBER: 140:59830

TITLE: Process for preparing fluticasone propionate from

flumethasone

INVENTOR(S): Jadav, Kanaksinh Jesingbhai; Kambhampati, Sudhakar;

Chitturi, Trinadha Rao; Thennati, Rajamannar PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Limited, India

SOURCE: PCT Int. Appl., 29 pp.

CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English

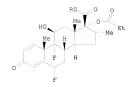
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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WO	2004							031231 WO 2003-IN219												
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AU	U 2003263575 P 1534733						20040106													
110		IE,	SI,	LT,	LV,	FI,	ES, RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	SK				
US	US 20050256325 US 7208613 RIORITY APPLN. INFO.:									IN 2 IN 2	002-	MU54	4	į	A 2		620			
									WO 2003-IN219					1	7 2	0030	616			

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): CASREACT 140:59830

GT



AB The present invention relates to a process for preparing fluticasone propionate [I; R = CH2F (II)] via (a) treating I [R = CONMe2 (III)] with alkali metal carbonate-alc. system to obtain I [R = H (IV)]; and (b) reacting IV with bromofluoromethane. The present invention also provides an improved process for preparation of II via reacting 6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-(propionyloxy) androsta-1, 4-dien-17β-carboxylic acid with N, N-dimethylthiocarbamoyl chloride in an inert aprotic solvent in the presence of an iodide catalyst and a base to give III and then reacting III with a hydrosulfide reagent and bromofluoromethane. Thus, flumethasone on oxidation with periodic acid afforded 6α,9α-difluoro-11β,17α-dihydroxy-16α-methyl-3oxo-androst-1,4-diene-17β-carboxylic acid which was reacted with propionic anhydride to provide 6α,9α-difluoro-11β-hydroxy-16α-methyl-17α-propionyloxy-3-oxo-androst-1,4-diene-17βcarboxylic acid (V). The intermediate V was reacted with N,N-dimethylthiocarbamoyl chloride to afford III which was treated with

Ι

bromofluoromethane yielded II.

11 80474-45-9P RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of fluticasone propionate from flumethasone)
RN 80474-45-9 CAPLUS

K2CO3 in methanol to give IV. Subsequent reaction between IV and

Androsta-1, 4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, $(6\alpha,11\beta,16\alpha,17\alpha)$ - (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

CN

IT 80474-14-2P, Fluticasone propionate

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of fluticasone propionate from flumethasone)

RN

80474-14-2 CAPLUS Androsta-1,4-diene-17-carbothioic acid, CN

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA

INDEX NAME)

Absolute stereochemistry.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L38 ANSWER 24 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:633732 CAPLUS

DOCUMENT NUMBER: 139:180234

TITLE: Process for the preparation of

6α,9α-difluoro-17α-(1-oxopropoxy-

 11β -hydroxy- 16α -methyl-3-oxo-androst-1,4-

APPLICATION NO.

DATE

diene-17β-carbothioic acid

KIND DATE

INVENTOR(S): Coote, Steven John; Nice, Rosalyn Kay; Wipperman, Mark

David

PATENT ASSIGNEE(S): Glaxo Group Limited, UK SOURCE: PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

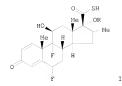
PATENT INFORMATION:

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WO	2003	0666	54		A1 20030814							20030203					
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		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC	, EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE	, KG,	KP,	KR,	KZ,	LC,	LK,	LR,
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AU	2003	2068	37		A1		2003	0902		AU :	2003-	20030203					
AU	2003	2068	37		B2		2008	1113									
EP	1472271				A1 20041103			EP 2003-704542									
	R:										, IT,						PT,
											, TR,						
BR	2003	0073.	52		A	2004	1214		BR :	2003-	7352	20030203					
CN	1628	125			A	2005	0615		CN :	2003-	8032	20030203					
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										WU.	2003-	FLTT	Тρ		w 2	0030	2U3

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 139:180234

GI



AB The present invention relates to a novel process for the synthesis of 6α , 9α -difluoro- 17α -(1-oxopropoxy)- 11β -hydroxy-

 16α -methyl-3-oxo-androst-1,4-diene-1'7B-carbothioic acid [I; R = COC2H5 [II]) or a salt thereof, useful in the preparation of anti-inflammatory steroids. Thus, I (R = H), in N,N-dimethylformamide, was treated with propionyl chloride to afford II in 83.7% yield.

IT 80474-14-2P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of difluorooxopropoxyhydroxymethyl oxoandrostdienecarbothioic acid S-fluoromethyl ester from difluorodihydroxymethyl oxoandrostdienecarbothioic acid)

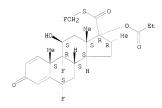
RN 80474-14-2 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-,

S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA INDEX NAME)

Absolute stereochemistry.



IT 80474-45-9P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of difluorooxopropoxyhydroxymethyl oxoandrostdienecarbothioic acid from difluorodihydroxymethyl oxoandrostdienecarbothioic acid)

RN 80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methy1-3-oxo-17-(1-oxopropoxy)-, (6 α ,11 β ,16 α ,17 α)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 25 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:633731 CAPLUS

DOCUMENT NUMBER: 139:180233

TITLE: Process for preparing fluticasone propionate

Coote, Steven John; Nice, Rosalyn Kay; Wipperman, Mark INVENTOR(S):

David

PATENT ASSIGNEE(S): Glaxo Group Limited, UK PCT Int. Appl., 26 pp.

SOURCE: CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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											TR,									
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										WO :	2003-	EP11	15		W 2	0030	203			

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 139:180233 GI

AB The present invention relates to a process for preparing fluticasone propionate [I, R = CH2F (II)] as crystalline polymorphic which comprises reacting I [R = H (III)] or a salt thereof with LCH2F (L = leaving group) optionally in the presence of a phase transfer catalyst, a water-immiscible non-solvating organic liquid solvent and water. Thus, 6α , 9α -difluoro-11 β , 17α -dihydroxy- 16α -methyl-3- ∞ -androst-1, 4-diene-17 β -carbothioic acid was reacted with propionyl chloride to provide III which was treated with bromofluoromethane in presence of benyltributylemmonium chloride and triethylamine using Et acetate as solvent and hexane as anti-solvent to afford II in 95.7% yield.

IT 80474-14-2P RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)

(preparation of fluticasone propionate from difluorodihydroxymethyl oxoandrostdienecarbothioic acid)

RN 80474-14-2 CAPLUS

Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, (6a,11β,16a,17a)- (CA INDEX NAME)

Absolute stereochemistry.

IT 80474-45-9P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of fluticasone propionate from difluorodihydroxymethyl

oxoandrostdienecarbothioic acid)

RN 80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6a,11B,16a,17a) - (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

REFERENCE COUNT:

3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L38 ANSWER 26 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:300611 CAPLUS

DOCUMENT NUMBER: 138:309306

TITLE: Formulation containing anti-inflammatory androstane derivatives

INVENTOR(S):

Biggadike, Keith; Sayani, Amyn P.; Buxton, Ian; Reed,

Kenton

PATENT ASSIGNEE(S):

U.S. Pat. Appl. Publ., 13 pp., Cont.-in-part of Ser. SOURCE:

No. US 2001-958050, filed on 2 Oct 2001

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 11 PATENT INFORMATION:

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US	2003	0073	676				2003	0417		US 2						0020	
	2634				A1		2004			CA 2	001-	2634	715		2	0010	803
	2002		65		A1		2002			WO 2	001-	GB34	95			0010	
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CN	1315	400			C		2007	0516		O17 0	0.0.5	1000	2000			0010	000
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ΕP	2067		,	,			2009						9		2	0010	803
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							IN,										
							MD,										
							SD, VN,					ıJ,	TU,	TIN,	IK,	11,	ız,
	DM.						MZ,					HC	7.M	7.W	ΔM	A 7	BV
	144.						TM,										

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                         A1 20030814 WO 2003-GB485 20030204
     WO 2003066033
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     AU 2003205850
                         A1 20030902 AU 2003-205850 20030204
A1 20030902 AU 2003-205855 20030204
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                                20080528
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     JP 2005523267
                          т
                             20050804 JP 2003-565451
                                                                    20030204
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EP 2006-124055
     JP 2005523268
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     AT 396716
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                                                                    20030204
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                                          ES 2003-702732
     ES 2305438
                          Т3
                                                                    20030204
                         A1 20050203
                                                                    20040813
     US 20050026888
                                           US 2004-918770
     US 7531528
                        B2 20090512
    US 20050175545 A1 20050811 US 2005-503540 US 20050209206 A1 20050922 US 2005-503000 JP 2010077145 A 20100408 JP 2009-265248
                                                                    20050325
                                                                    20050414
                                                                    20091120
PRIORITY APPLN. INFO.:
                                            GB 2000-19172
                                                               A 20000805
                                            WO 2001-GB3495
                                                               A1 20010803
                                            US 2001-958050
                                                                A2 20011002
                                            GB 2001-8800
                                                                A 20010407
                                                               A3 20010803
                                            CA 2001-2417825
                                            CN 2001-816662
                                                               A3 20010803
                                            CN 2001-816664
                                                                A3 20010803
                                            EP 2001-953272
                                                                A3 20010803
                                            EP 2001-954149
                                                                A3 20010803
                                            JP 2002-518238
                                                                A3 20010803
                                            US 2002-66951
                                                                A 20020204
                                            US 2002-66961
                                                                A 20020204
                                            EP 2003-702732
                                                                A3 20030204
                                            WO 2003-GB469
                                                                W 20030204
                                                                W 20030204
                                            WO 2003-GB485
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OTHER SOURCE(S): MARPAT 138:309306

AB There is provided according to the invention a pharmaceutical formulation comprising an aqueous carrier liquid having dissolved therein (a) an ester of fluticasone or a solvate thereof as medicament and (b) a solubilizing agent for assisting the solubilization of the medicament in the aqueous carrier liquid For example, a formulation for intransal delivery contained fluticasone propionate 0.05%, Triton X-1005 4%dextrose 4%, BKC 0.015%, BDTA 0.015%, and water to 100%. The solution obtained was filled into a

bottle fitted with a metering valve adapted to dispense $50\text{--}100~\mu\text{l}$ per actuation.

T 80474-14-2P, Fluticasone propionate

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (solubilization of anti-inflammatory androstane derivs. for liquid

(solubilization of anti-inflammatory androstane derivs, for liquid formulations)

RN 80474-14-2 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA

INDEX NAME)

Absolute stereochemistry.

3

OS.CITING REF COUNT:

- THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
- REFERENCE COUNT:
- 162 THERE ARE 162 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 27 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:132962 CAPLUS

DOCUMENT NUMBER: 138:170401

TITLE: A method for preparing fluticasone derivatives Partridge, John Joseph; Walker, Dwight Sherod INVENTOR(S):

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2 DOCUMENT TYPE:

Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

	ENT				KIN	D	DATE			APPL	ICAT				D.	ATE	
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WO	2003	0134	27		A3		2003	1016									
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		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
		PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TN,	TR,	TT,	TZ,
		UA,	UG,	US,	UZ,	VN,	YU,	ZA,	ZM,	ZW							
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,
		KG,	KZ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		FI,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,	SK,	TR,	BF,	BJ,	CF,
		CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG			
AU	2002	3218	84		A1		2003	0224		AU 2	002-	3218	84		2	0020	801
PRIORITY	APP	LN.	INFO	. :						US 2	001-	3673	41P		P 2	0010	803
										WO 2	002-	US24	586		W 2	0020	801
OTHER SO	URCE	(S):			CAS	REAC	T 13	8:17	0401								

AΒ A method was developed for preparing 6α,9α-difluoro-17α-[(2furanylcarbonyl)oxy]-11β-hydroxy-16α-methyl-3-oxoandrosta-1,4diene-β-carbothioic acid S-fluoromethyl ester by reacting the thiocarboxylic acid with a solution containing chlorofluoromethane and a mild base medium at a temperature in the range of -20° C to 60° C. Thus, the thioacid furoate I (R = H) was treated with C1CH2F in DMF containing NaI and KHCO3 at -15° for 15m and then warmed to 15° ≥ 15m to give 82.6 % I (R = CH2F). 80474-14-2P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(method for preparing fluticasone derivs.)

RN 80474-14-2 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, (6a,11B,16a,17a)- (CA

INDEX NAME)

Absolute stereochemistry.

IT 80474-45-9

RL: RCT (Reactant); RACT (Reactant or reagent) (method for preparing fluticasone derivs.)

RN 80474-45-9 CAPLUS

CN Androsta-1,4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, $(6\alpha,11\beta,16\alpha,17\alpha)$ - (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

OS.CITING REF COUNT:

THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD
(6 CITINGS)

REFERENCE COUNT:

4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L38 ANSWER 28 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2002:90061 CAPLUS

DOCUMENT NUMBER: 136:134954

TITLE: Preparation of the anti-inflammatory steroid

intermediate 6a,9a-difluoro-

11β,17α-dihydroxy-16α-methylandrosta-

1,4-dien-3-one-17β-carboxylic acid via a novel oxidation process

INVENTOR(S): Albinson, Frederick David; Coote, Steven John;

Robinson, John Malcolm PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION:

PAT	TENT	NO.			KIN	D	DATE			API	PLI	CAT	ION :	NO.		D.	ATE	
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							DK,											
							IN,											
							MD,											
							SI,											
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	RW:	GH.	GM.	KE.	LS.	MW.	MZ.	SD.	SL.	S	Ζ.	TZ.	UG.	ZW.	AT.	BE.	CH.	CY.
							GB,											
							GA,											
CA	2406				A1		2002	0131		CA	20	01-	2406	963		2	0010	720
EP	1301	526			A1		2002 2003	0416		EP	20	01-	9497	91		2	0010	720
EP	1301	526			B1		2008	0618										
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		ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	ΑI	١,	TR						
BR	2001	0104	30		A		2003	0708		BR	20	01-	1043	0		2	0010	720
HU	2003	0011	08		A2		2003	0828		HU	20	03-	1108			2	0010	720
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JP	2004	5044	03		T		2004	0212		JP	20	02-	5141	48		2	0010	720
NZ	5220	83			A		2004	0625		NZ	20	01-	5220	83		2	0010	720
AU	2001	2709	06		B2		2005	1013		ΑU	20	01-	2709	06		2	0010	720
CN	2001 1315 3986 1523 2307 2002	864			С		2007	0516		CN	20	01-	8114	40		2	0010	720
ΑT	3986	28			T		2008	0715		ΑT	20	01-	9497	91		2	0010	720
IL	1523	48			A		2008	0807		IL	20	01-	1523	48		2	0010	720
ES	2307	628			Т3		2008	1201		ES	20	01-	9497	91		2	0010	720
ZA	2002	0083	72		A		2004	0211		ZA	20	002-	8372			2	0021	017
TIA	2002	L/M/A/T	202		22		2005	0211										
NO	2002	0050	54		A		2002			ИО	20	002-	5054			2	0021	021
	3248	36			B1		2007											
	7872	93			B1		2007	1220		KR	20	002-	7143	67		2	0021	025
MX	2002	0109	67		A		2003	0327		MX	20	002-	1096	7_		2	0021	107
US	2004	0043	974		A1		2004	0304		US	20	003-	3335	37		2	0030	815
HK	1056	179			A1		2009	0717		HK	20	103-	1066	80		_ 2	0030	917
RIT	2004 1056 APP	LN.	INFO	.:						GB	20	100-	1798	8		A 2	0000	721
										WO	20	101-	GB32	89		w 2	UU10	/20

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 136:134954

G1

AB The present invention relates to a novel oxidation process for the synthesis of a known intermediate (1), useful in the preparation of anti-inflammatory steroids. Thus, flumethasone in THF was treated with an aqueous solution of periodic acid to give I in 98% yield.

IT 80474-45-9P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of difluorodihydroxymethyl androstadienonecarboxylic acid via a novel oxidation process)

RN 80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

Ι

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, $(6\alpha,11\beta,16\alpha,17\alpha)$ - (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 80474-14-2P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of difluorodihydroxymethyl androstadienonecarboxylic acid via a novel oxidation process)

RN 80474-14-2 CAPLUS

Androsta-1, 4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-,

S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA

INDEX NAME)

Absolute stereochemistry.

OS.CITING REF COUNT:

THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT:

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 29 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2001:636040 CAPLUS

DOCUMENT NUMBER: 135:211173

TITLE: Method for the preparation of fluticasone and related

17β-carbothioic esters using a novel carbothioic acid synthesis and novel purification methods
INVENTOR(5): Barkalow, Jufang; Chamberlin, Steven A.; Cooper,

Arthur J.; Hossain, Azad; Hufnagel, John J.; Langridge, Denton C.

PATENT ASSIGNEE(S): Abbott Laboratories, USA SOURCE: PCT Int. Appl., 33 pp.

SOURCE: PCT Int. Appl., 3
CODEN: PIXXD2
DOCUMENT TYPE: Patent

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

	TENT :																ATE	
WO WO	2001 2001 W:	0627 0627	22 22		A2 A3		2001	0830	1								0010	223
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US	2002	0133	032		A1		2002	0919	1	US	200	0 - 5	133	99		2	0000	225
CA	2400	919			A1		2001	0830										
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EP	1257	531			A2		2002	1120	1	EΡ	200	1-9	162	31		2	0010	223
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JP	2003	5295	64		T		2003	1007		JP	200	1-5	617	31		2	0010	223
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PT	1257	531			E		2005	0131	1	PT	200	1-9	162	31		2	0010	223
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	2002							0128	1	MΧ	200	2-8	275			2	0020	823
US	2004	0209	854		A1		2004	1021	1	US	200	4-8	478	46		2	0040	518
US	7214	807			B2		2007	0508										
PRIORIT	Y APP	LN.	INFO	. :					1	US	200	0-5	133	99	Z	A 2	0000	225
															Ţ			

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): CASREACT 135:211173; MARPAT 135:211173

GI

- AB A method for converting a carboxylic acid to a carbothioic acid group I (R and Rl independently are Cl-6 alkyl or R and Rl independently are Cl-6 alkylene) was accomplished. This method was used for the conversion of carboxylic acids to carbothioic acids, and for both the preparation of androstane 179-carbothioic acids and fluticasone propionate which avoided the use of column chromatog. Thus II was prepared from flumethasone reacted in Pd(II) acetate and PPh3 in DMA yielding the 179-carboxylic acid which was treated with propionyl chloride followed by N,N-dimethylthiocarbamoyl chloride and then chlorofluoromethane yielding II in 70%.
 - T 80474-14-2P, Fluticasone propionate 80474-45-9DP, salts
 - RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of androstane 17B-carbothioic esters)
- RN 80474-14-2 CAPLUS
- NAME OF THE CARDON OF T

Absolute stereochemistry.

- RN 80474-45-9 CAPLUS
- CN Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6a,118,16a,17a)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

13

- OS.CITING REF COUNT:
- REFERENCE COUNT:
- THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
- THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 30 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1998:706263 CAPLUS

DOCUMENT NUMBER: 129:276096 ORIGINAL REFERENCE NO.: 129:56305a

TITLE: Process for the manufacture of

androstane-17-carbothioates via esterification with

halofluoromethanes
INVENTOR(S): Cherkez, Stephen

PATENT ASSIGNEE(S): Chemagis Ltd., Israel

SOURCE: Israeli, 15 pp.
CODEN: ISXXAQ

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
				-	
IL 109656	A	19980222	IL 1994-109656		19940515
IN 185691	A1	20010407	IN 1994-DE1716		19941230
PRIORITY APPLN. INFO.:			IL 1994-109656	Α	19940515
OTHER SOURCE(S):	CASREA	CT 129:27609	6; MARPAT 129:276096		

0 SR1
HO Me OR2
R3

AB A process for the preparation of an androstane-17-carbothiolc ester I [R1 = fluoromethyl, difluoromethyl, trifluoromethyl, R2 = COR6, R6 = C1-3-alkyl; R3 = H, α -Me, β -Me, methylene; R = H, Cl, F; R5 = H, F; dotted line = single or double bond] by the direct esterification of a corresponding androstane-17-carbothioic acid I [R1 = H] with a halofluoromethane of formula XCH2F, XCH2P or XCF3 [X = Br, Cl] and optionally in the presence of a catalyst is claimed. Thus, fluticasone propionate (I; R1 = CH2F, R2 = COSt, R3 = Me, R4 = R5 = Me, dashed line = double bond) was prepared via esterification of I (R1 = H, R2 = COSt, R3 = Me, R4 = R5 = Me, dashed and catalytic Bu4NBr.

IT 80474-45-9

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of androstane-17-carbothioates via esterification with halofluoromethanes)

RN 80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6α, 11β, 16α, 17α) - (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

- IT 80474-14-2P, Fluticasone propionate RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of androstane-17-carbothioates via esterification with halofluoromethanes)
- RN 80474-14-2 CAPLUS
- CN Androsta-1, 4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, (6a,11β,16a,17a)- (CA INDEX NAME)

Absolute stereochemistry.

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

L38 ANSWER 31 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN ACCESSION NUMBER: 1997:454923 CAPLUS DOCUMENT NUMBER: 127:95446

ORIGINAL REFERENCE NO.: 127:18381a,18384a

TITLE: Automated radiosynthesis of no-carrier-added
[S-fluoromethyl-18F]fluticasone propionate as a

radiotracer for lung deposition studies with PET
AUTHOR(S): Aigbirhio, Franklin I.; Carr, Richard M.; Pike, Victor

W.; Steel, Colin J.; Sutherland, Derek R.
CORPORATE SOURCE: Chemistry and Engineering Group, MRC Cyclotron Unit,

Royal Postgraduate Medical School, Hammersmith

Hospital, London, W12 ONN, UK
SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals

(1997), 39(7), 567-584

CODEN: JLCRD4; ISSN: 0362-4803

PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fluticasone propionate [(S)-fluoromethyl-6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-(propionyloxy)-androsta-

11β-hydroxy-16d-methyl-3-oxo-17d-(propionyloxy)-androsta-1,4-diene-17β-carbothioate: FP] is a potent anti-inflammatory steroid with several therapeutic indications, including use as an anti-asthmatic drug when administered as sized particles by inhalation from a pressurized metered-dose inhaler (pMDI). FP was successfully labeled with fluorine-18 (t1/2 = 109.6 min; β_1 = 100%) by displacement of tosylate with cyclotron-produced no-carrier-added [18F]fluoride in an (S)-tosylmethyl precursor prepared from the known (S)-chloromethyl analog of FP. Radiochem. pure [S-fluoromethyl-18F]FF was separated by reverse phase HPLC in 35% radiochem. yield (decay-corrected) within 80 min from the end of radionuclide production (as verified by, radio-HPLC, LC-MS and LC-NMR). The radiosynthesis was automated for the safe production of high radioactivities (20-50 mCl) of [18F]FF in a lead-shielded hot-cell for subsequent incorporation into formulated FP particles within a pMDI and subsequent study of FP

deposition in human lung using positron emission tomog. (PET). IT 80474-14-2P

CM

RL: SPN (Synthetic preparation); PREP (Preparation)
(automated radiosynthesis of no carrier added
[S-fluoromethyl-18F]fluticasone propionate)

RN 80474-14-2 CAPLUS

Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, (6a,11\beta,16a,17a)- (CA INDEX NAME)

Absolute stereochemistry.

- OS.CITING REF COUNT:
- REFERENCE COUNT:
- 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS
- RECORD (13 CITINGS)

 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 32 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN ACCESSION NUMBER: 1996:681432 CAPLUS

DOCUMENT NUMBER: 126:19098

ORIGINAL REFERENCE NO.: 126:3969a,3972a
TITLE: Anti-inflammatory

17β-Thioalkyl-16α,17α-ketal and

-acetal Androstanes: A New Class of Airway Selective

Steroids for the Treatment of Asthma
AUTHOR(S): Ashton, Michael J.: Lawrence, Christo

Ashton, Michael J.; Lawrence, Christopher; Karlsson, Jan-Anders; Stuttle, Keith A. J.; Newton, Christopher G.; Vacher, Bernard Y. J.; Webber, Stephen; Withnall,

Michael J.

CORPORATE SOURCE: Dagenham Research Centre, Rhone-Poulenc Rorer Central

Research, Dagenham/Essex, RM10 7XS, UK Journal of Medicinal Chemistry (1996), 39(25),

4888-4896

CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English
OTHER SOURCE(S): CASREACT 126:19098

GI

SOURCE:

,

The synthesis and anti-inflammatory potencies of a new class of 17β-thioalkvl-16α,17α-ketal and -acetal androstanes, e.g. I [R1 - R3 = Me, X = H, F; R1 = H, R2 = Pr, R3 = Me, X = H, F; R1 = X = H, R2 = Pr, R3 = Et, CHMe2; R1 = X = H, R2 = (E)-CH:CHMe, R3 = Me], are described. This new class of steroids was made by fragmentation of 2-thioxo-1, 2-dihydropyrid-1-yl esters of the corresponding 17-acids to the 17-radical. The radical generated was trapped using a variety of radicophilic disulfides, giving a steroidal D-ring having acetal or ketal functionality at C-16 and C-17, together with a sulfide link at C-17. Compds. from this series bind to the glucocorticoid receptor with high potency and are functional agonists as measured by their ability to induce tyrosine aminotransferase activity in a rat hepatic cell line in vitro. These 17β-thioalkyl androstanes potently inhibit Sephadex-induced rat lung inflammation when administered directly into the airways. The high topical potency, together with a low propensity to induce systemic glucocorticoid-like side effects (rat thymus involution), provides the present compds. with a high degree of airway selectivity compared with currently available inhaled glucocorticoids. The presently described 17β -thioalkyl- 16α , 17α -ketal androstanes may be useful for therapies for inflammatory diseases such as asthma.

IT 80474-14-2DP, Fluticasone propionate, analogs RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (synthesis and antiinflammatory potencies of thioalkylandrostanediol

(synthesis and antiinflammatory potencies of thioalkylandrostanedio ketals and acetals)

RN 80474-14-2 CAPLUS

Not 1973-14-2 Galact
Not

Absolute stereochemistry.

27

14

OS.CITING REF COUNT:

THERE ARE 27 CAPLUS RECORDS THAT CITE THIS RECORD (27 CITINGS)

REFERENCE COUNT:

THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L38 ANSWER 33 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:
                        1995:64934 CAPLUS
DOCUMENT NUMBER:
                         122:81726
ORIGINAL REFERENCE NO.: 122:15539a,15542a
                        Synthesis and Structure-Activity Relationships in a
TITLE:
                         Series of Antiinflammatory Corticosteroid Analogs,
                         Halomethyl Androstane-17β-carbothioates and
                         -17B-carboselenoates
AUTHOR(S):
                        Phillipps, Gordon H.; Bailev, Esme J.; Bain, Brian M.;
                         Borella, Raymond A.; Buckton, Jacky B.; Clark, John
                         C.; Doherty, Alice E.; English, Alan F.; Fazakerley,
                         Harold; et al.
CORPORATE SOURCE:
                        Glaxo Research and Development Limited, Greenford/
                        Middlesex, UB6 OHE, UK
                        Journal of Medicinal Chemistry (1994), 37(22), 3717-29
SOURCE:
                         CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE:
                         Journal
LANGUAGE:
                         English
    The preparation and topical antiinflammatory potencies of a series of
     halomethyl 17a-(acyloxy)-11B-hydroxy-3-oxoandrosta-1,4-diene-
     17β-carbothicates, carrying combinations of 6α-fluoro,
     9a-fluoro, 16-Me, and 16-methylene substituents, are described. Key
     synthetic stages were the preparation of carbothioic acids and their reaction
     with dihalomethanes. The carbothioic acids were formed from
     17β-carboxylic acids by initial reaction with dimethylthiocarbamoyl
     chloride followed by aminolysis of the resulting rearranged mixed
     anhydride with diethylamine, or by carboxyl activation with
     1,1 -carbonyldiimidazole (CDI) or 2-fluoro-N-methylpyridiniumtosylate
     (FMPT) and reaction with hydrogen sulfide, the choice of reagent being
     governed by the 17\alpha-substituent. Carboxyl activation with FMPT and
     reaction with sodium hydrogen selenide led to the halomethyl
     16-methyleneandrostane-17β-carboselenoate analogs. Antiinflammatory
     potencies were measured in humans using the vasoconstriction assay and in
     rats and mice by a modification the Tonelli croton oil ear assay. Best
     activities were shown by fluoromethyl and chloromethyl carbothioates with
     a 17a-propionyloxy group. S-Fluoromethyl
     6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-
     17α-(propionyloxy)androsta-1,4-diene-17β-carbothioate
     (fluticasone propionate, FP) was selected for clin. study as it showed
     high topical antiinflammatory activity but caused little
     hypothalamic-pituitary-adrenal suppression after topical or oral
    administration to rodents.
    80474-14-2P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); BIOL (Biological
     study); PREP (Preparation)
        (synthesis and structure-activity relationships in a series of
        antiinflammatory corticosteroid analogs and halomethyl
        androstane-17\beta-carbothioates and -17\beta-carboselenoates)
RN
    80474-14-2 CAPLUS
    Androsta-1, 4-diene-17-carbothioic acid,
     6,9-difluoro-11-hvdroxv-16-methvl-3-oxo-17-(1-oxopropoxv)-,
     S-(fluoromethyl) ester, (6\alpha, 11\beta, 16\alpha, 17\alpha)- (CA
     INDEX NAME)
```

Absolute stereochemistry.

IT 80474-45-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and structure-activity relationships in a series of antiinflammatory corticosteroid analogs and halomethyl androstane-170-carbothioates and -170-carboselenoates)

RN 80474-45-9 CAPLUS

CN Androsta-1,4-diene-17-carbothioic acid,
6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-,
(6a,11B,16a,17a)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

OS.CITING REF COUNT: 32 THERE ARE 32 CAPLUS RECORDS THAT CITE THIS RECORD (32 CITINGS)

Page 132

L38 ANSWER 34 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN 1992:503834 CAPLUS

ACCESSION NUMBER: DOCUMENT NUMBER:

117:103834

ORIGINAL REFERENCE NO.: 117:17853a,17856a

TITLE: Antigenicity studies on fluticasone propionate

AUTHOR(S): Takeda, Kenzo; Fukuda, Ichiro; Nagamichi, Tameichiro;

Morida, Ken; Tomida, Mitsuvo; Okumura, Kazuo CORPORATE SOURCE: Tsukuba Res. Lab., Nippon Glaxo Ltd., Japan

SOURCE: Yakuri to Chiryo (1973-2000) (1992), 20(5), 1657-68

CODEN: YACHDS; ISSN: 0386-3603

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

Fluticasone propionate (FP) is a synthetic steroid used in the treatment of allergic nose and bronchial asthma. The antigenicity studies on FP and its protein conjugates (with cytochrome c and human serum albumin) in quinea pigs and rabbits were performed by active systemic anaphylaxis (ASA) test, homologous passive cutaneous anaphylaxis (PCA) test, and hemagglutination (HA) test. The results showed that FP and its protein conjugates had no antigenic activity under the exptl. conditions.

80474-14-2DP, Fluticasone propionate, conjugates with cytochrome

c and human serum albumin RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and antigenicity of)

80474-14-2 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-,

S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA

INDEX NAME)

Absolute stereochemistry.

L38 ANSWER 35 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1986:406673 CAPLUS DOCUMENT NUMBER: 105:6673

ORIGINAL REFERENCE NO.: 105:1245a,1248a

Thiol esters from steroid 17β-carboxylic acids: TITLE: carboxylate activation and internal participation by

17α-acvlates

AUTHOR(S): Kertesz, Denis J.; Marx, Michael

CORPORATE SOURCE: Syntex Res., Palo Alto, CA, 94304, USA

Journal of Organic Chemistry (1986), 51(12), 2315-28 SOURCE:

CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 105:6673

GT

Pregnene-17 β -carboxylic acids, e.g., I (R, R1, R2 = F, F, H0; H, F, AB HO; F, Cl, Cl) derived from 16,17α-disubstituted corticosteroids were converted into thiol esters. Major quantities of spiro byproducts e.g. II (R = R1 = F, R2 = HO) were observed in the reaction of $16-methyl-17\alpha-acyloxy$ acids, and the degree of 17-esterparticipation leading to these structures was dependent on the carboxylate activating group used and stereochem. at C-16. Di-Et phosphate mixed anhydrides of these acids reacted with mercaptide salts to give mixts. of thiol esters with spiro acylthio ortho esters, which predominated and were particularly stable in the case of 16β-Me substrates; in addition, considerable reversion of 16α-Me phosphate intermediates to starting acid was experienced. The use of di-Ph chlorophosphate as the activating

agent greatly improved yields of thiol esters. Methanolysis of the phosphate adducts derived from 17a-acyloxy acids gave spiro acyl ortho esters as the exclusive products. The reactions of 17a-acetoxy acids with 2-fluoro-N-methylpyridinium tosylate (III) gave novel spiro acyl fluoro ketals, e.g., IV (R = R1 = F; R2 = HO) whereas similar treatment of 17-hydroxy acids led to products of dehydration or of 18-Me migration, e.g., lactone V. Activation was carbonyldiimidazole followed by addition of mercaptans allowed the preparation

of

thiol ester products from 17-hydroxy acids, but the method was restricted to use with these substrates. Neighboring-group participation was not possible for the 16,17-acetonide acid VI, and activation with either chlorophosphate diesters or III followed by reaction with MeS- gave high yields of methylthio ester VII.

тт 73205-13-7P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)

RN 73205-13-7 CAPLUS

CN

Androsta-1, 4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-methyl ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA INDEX NAME)

Absolute stereochemistry.

OS.CITING REF COUNT:

19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)

L38 ANSWER 36 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1982:163044 CAPLUS DOCUMENT NUMBER: 96:163044

ORIGINAL REFERENCE NO.: 96:26859a,26862a

Androstane carbothioates PATENT ASSIGNEE(S): Glaxo Group Ltd., UK SOURCE: Neth. Appl., 63 pp. CODEN: NAXXAN

DOCUMENT TYPE: Patent LANGUAGE: Dutch

FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 8100707	A	19810916	NL 1981-707	19810213
NL 191792	B	19960401		
NL 191792	C	19960802		
BE 887518	A1	19810813	BE 1981-203794	19810213
DK 8100623	A	19810816	DK 1981-623	19810213
DK 147022	В	19840319		
DK 147022	C	19840827		
FI 8100444	A	19810816	FI 1981-444	19810213
FI 70904	В	19860718		
FI 70904	С	19861027		
SE 8101010	A	19810816	SE 1981-1010	19810213
SE 452468	В	19871130		
SE 452468	C	19880310		
AU 8167298	A	19810820	AU 1981-67298	19810213
AU 544517	B2	19850606		
FR 2477156	A1	19810904	FR 1981-2818	19810213
FR 2477156	B1	19841116		
JP 56138200	A	19811028	JP 1981-20790	19810213
JP 63037120	В	19880722	DB 4004 0405007	40040040
DE 3105307	A1	19811210	DE 1981-3105307	19810213
DE 3105307 US 4335121	C2	19880929	770 1001 0011110	10010010
GB 2088877	A A	19820615 19820616	US 1981-234113 GB 1981-4496	19810213 19810213
GB 2088877	B	19840704	GB 1981-4496	19810213
ZA 8100976	A A	19840704	ZA 1981-976	19810213
CH 644615	A5	19840815	CH 1981-982	19810213
CH 651307	A5	19850913	CH 1984-3890	19810213
AT 8100674	A	19920515	AT 1981-674	19810213
AT 395427	B	19921228	A1 1901-074	19010213
DE 3153379	C2	19921228	DE 1981-3153379	19810213
FR 2485542	A1	19811231	FR 1981-15812	19810817
FR 2485542	B1	19830610	FK 1901-13012	13010017
US 4578221	A	19860325	US 1983-513396	19830714
GB 2137206	A	19841003	GB 1983-25400	19830922
GB 2137206	В	19850403	OB 1700 D0100	13000300
AT 8400170	A	19920515	AT 1984-170	19840119
AT 395428	В	19921228		27010227
US 4650610	A	19870317	US 1985-753428	19850710
AT 8602031	A	19920515	AT 1986-2031	19860728
AT 395429	В	19921228		
AT 9100344	A	19960215	AT 1991-344	19910219
AT 401521	В	19960925		

SK 278140 CZ 281275		B6 B6	19960207 19960814		1991-4034 1991-4034		19911223 19911223
PRIORITY APPLN.	INFO.:	Do	13300014		1980-5174	Α	19800215
				GB	1980-13339	Α	19800423
				ΑT	1981-674	A	19810213
				CH	1981-982	Α	19810213
				GB	1981-4496	A3	19810213
				US	1981-256845	A1	19810423
				US	1982-408837	A1	19820817
				US	1983-513396	A1	19830714

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): CASREACT 96:163044; MARPAT 96:163044 GI

- AB Antiinflammatory (no data) androstanes I (R = CH2F, CH2Cl, CH2Br, CH2CH2F; R1 = acyl, R1R2 = CH2C); R2 = H, α or β -Me, R7 = H; R2R7 = CH2; R3 = H, Cl, F; R4 = H, F; R5 = R6 = H; R5R6 = bond) were prepared Thus, I (R = CH2Cl, R1 = COEt, R2 = β -Me, R3 = F, R4 = H, R5R6 = bond, R7 = H) was prepared by treating the corresponding 17-carboxylic acid with Me2NCSCl, hydrolyzing to the 17-thiocarboxylic acid, and esterifying with
- BrCHZC1.

 180474-45-9P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 - (preparation and esterification of)
- RN 80474-45-9 CAPLUS CN Androsta-1,4-diene-1
 - Androsta-1, 4-diene-l7-carbothioic acid, 6,9-difluoro-l1-hydroxy-l6-methyl-3-oxo-l7-(l-oxopropoxy)-, (6 α ,11 β ,16 α ,17 α) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

80474-14-2P ΙT

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)

- RN
- 80474-14-2 CAPLUS Androsta-1,4-diene-17-carbothioic acid, CN 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, $(6\alpha, 11\beta, 16\alpha, 17\alpha)$ - (CA INDEX NAME)

Absolute stereochemistry.

OS.CITING REF COUNT: 29 THERE ARE 29 CAPLUS RECORDS THAT CITE THIS RECORD (31 CITINGS)

L38 ANSWER 37 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1980:447002 CAPLUS

DOCUMENT NUMBER: 93:47002

ORIGINAL REFERENCE NO.: 93:7791a,7794a

TITLE: Thioetianic acid derivatives INVENTOR(S):

Edwards, John A.

PATENT ASSIGNEE(S): Syntex (U.S.A.), Inc., USA

Brit. UK Pat. Appl., 14 pp. SOURCE:

CODEN: BAXXDU DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	API	PLICATION NO.		DATE
GB 2018256 GB 2018256 US 4188385 EP 4741 EP 4741	A	19791017	GB	1979-10862	_	19790328
GB 2018256	В	19830202 19800212	***	1000 000000		201100101
US 4188385	A		05	1978-893388		19780405
EP 4741	AZ	19791017 19791114	EP	1979-300500		19/90328
EP 4741 EP 4741	B1	19810128				
			,			
R: BE, CH, DE, DE 2912331	A1	, 11, NL, SE 19791018	ם כ	1979-2912331		19790328
FR 2421912		19791018		1979-2912331		19790328
FR 2421912 FR 2421912			PR	19/9-/823		19/90328
FR 2421912	BI	19810320 19791018		1979-45583		19790329
AU /943363	N N	19821216	AU	19/9-45565		19/90329
AU 326023	B2 B2	19821216	00	1070 2107		19790329
TT E6072	3	19820131	TI	1979-2107 1979-56972		19790329
CA 1134345	2.1	19821026	117	1979-30972		19790329
CA 1134343	AI	19791006	ET	1979-324557 1979-1081		19790330
E1 /901061	A D	19840629	гı	19/9-1001		19/90402
FA 2421912 AU 7945583 AU 526025 CS 203956 IL 56972 CA 1134345 FI 7901081 FI 66393 FI 66393	C	19841010				
DK 7901364	70	19791006	DK	1979-1365		19790403
DK 147735	B	19841126	511	1979 1303		15,50105
DK 147735	č	19850819				
FI 66393 DK 7901364 DK 147735 DK 147735 HU 21686 HU 179314	A2	19820128	HU	1979-SI1682		19790403
HU 179314	В	19820928				
NO 7901140	A	19791008	NO	1979-1140		19790404
NO 152935	В	19850909				
	С	19851218				
AT 7902519	A	19820115	AT	1979-2519		19790404
AT 368168	В	19820927				
PL 121469 SU 1052161	B1	19820531	PL	1979-214676		19790404
SU 1052161	A3	19831030	SU	1979-214676 1979-2787402		19790404
JP 54141758	B B1 A3 A B	19791105	JP	1979-40414		19790405
JP 61001038	В	19860113				
ZA 7901635	A	19801126	ZA	1979-1635		19790405
JP 60069019		19850419	JP	1984-155726		19840727
	В	19860910				
PRIORITY APPLN. INFO.:			US	1978-893388	Α	19780405
0.7			US	1978-893390	A	19780405

AB Steroids I (R = H, F, Cl; Rl = H, F, Cl, Br; R2R3 = O; R2 = OH, Cl, R3 = H; R4 = Cl-6 alkyl, Ph or PhCH2 optionally substituted on the ring by Cl-4 alkyl, Cl-4 alkoxy, halo; R5 = H, C2-6 alkanoyl; R6 = H, α-Me, β-Me, ORSR6 = 16α,17α-isopropylidenedioxy), useful as inflammation inhibitors, were prepared from the corresponding 17β-carboxylic acids or their reactive derivs. by treatment with alkali metal salts of R4R1. Thus, Me 6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-propionyloxyandroxta-1,4-diene-17β-thiocarboxylate (II) was prepared from flumethasone by sequential treatment with K2CO3/MeOH/air (room temperature, 1 atm, 22 h), (EtCO)2O, (EtC)2P(O)Cl, and MeSH/NaH. The topical antiinflammatory activity of II was assessed in humans by vasoconstriction

assay; potency was excellent with little or no systemic activity.

17 73205-13-7P
RL: SPN (Synthetic preparation); PREP (Preparation)

Ι

(preparation of, as inflammation inhibitor) RN 73205-13-7 CAPLUS

CN

Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-methyl ester, (6a,118,16a,17a)- (CA INDEX NAME)

Absolute stereochemistry.

OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)

L38 ANSWER 38 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1980:426654 CAPLUS DOCUMENT NUMBER: 93:26654

DOCUMENT NUMBER: 93:26654
ORIGINAL REFERENCE NO.: 93:4485a,4488a

ORIGINAL REFERENCE NO.: 93:4485a,4488a

TITLE: 17β -Thiocarboxylic acid esters of 6α , 6β -difluoro-3-oxoandrost-4-enes

INVENTOR(S): Edwards, John A.

PATENT ASSIGNEE(S): Syntex (U.S.A.), Inc., USA

Ι

SOURCE: U.S., 18 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4187301	A	19800205	US 1978-893389	19780405
PRIORITY APPLN. INFO.:			US 1978-893389	19780405
OTHER SOURCE(S):	MARPAT	93:26654		
CT				

AB Antiinflammatory (no data) androstenethiocarboxylates I [R = H, F, Cl, Br; R1R2 = O, H,OH, Cl; R3 = Cl-6 alkyl, Ph, PhCH2 (Ph substituted by Cl-4 alkyl, Cl-4 alkoxy, halo); R4 = OH, C2-6 alkanoyloxy; R5 = H, α-Me, β-Me; R4R5 = CCMe2O] and 1,2-didehydro derivs. of I were prepared Thus, oxidation of flumethasone followed by conversion to dismixed anhydride by the addition of (EtO)2P(O)Cl and then reaction with NaH-Me2S gave Me 6u,9-difluoro-1lβ-hydroxy-16α-methyl-3-oxo-1/α- (propionyloxy) androsta-1,4-diene-17β-hydroxy-16α-briocarboxylate.

IT 73205-13-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and methylation of)

(preparation and methyration

RN 73205-13-7 CAPLUS

CN Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-methyl ester, (6a,11B,16a,17a) - (CA INDEX NAME)

Absolute stereochemistry.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

L38 ANSWER 39 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN ACCESSION NUMBER: 1980:147047 CAPLUS

DOCUMENT NUMBER: 92:147047

ORIGINAL REFERENCE NO.: 92:23913a,23916a

TITLE: 17β-Thiocarboxylic acid esters of

4-halo-3-oxoandrost-4-enes INVENTOR(S): Alvarez, Francisco S.

PATENT ASSIGNEE(S): Syntex (U.S.A.), Inc., USA SOURCE: Eur. Pat. Appl., 60 pp.

CODEN: EPXXDW
DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 4773 EP 4773	A2 A3	19791017 19791031	EP 1979-300549	-	19790403
EP 4773 R: BE, CH, DE,	B1 FR, GB	19810429 , NL, SE			
US 4198403	A	19800415	US 1978-893390		19780405
FI 7901088	A	19791006	FI 1979-1088		19790402
IL 56991	A	19820131	IL 1979-56991		19790402
DK 7901364	A	19791006	DK 1979-1365		19790403
DK 147735	В	19841126			
DK 147735	С	19850819			
AU 7945752	A	19791011	AU 1979-45752		19790403
NO 7901141	A	19791008	NO 1979-1141		19790404
PL 118567	B1	19811031	PL 1979-214675		19790404
CS 209916	B2	19811231	CS 1979-2306		19790404
CS 209919	B2	19811231	CS 1979-7273		19790404
AT 7902518	A	19820415	AT 1979-2518		19790404
PL 121569	B1	19820531	PL 1979-222926		19790404
JP 54135761	A	19791022	JP 1979-40413		19790405
ZA 7901638	A	19801126	ZA 1979-1638		19790405
PRIORITY APPLN. INFO.:			US 1978-893390		19780405
			US 1978-893388	Α	19780405

OTHER SOURCE(S): MARPAT 92:147047

AB Antiinflammatory androstenethicoarboxylates I (R = Cl-6 alkyl, alkyl-alkoxy-halo-substituted Ph or PhCH2; RI = H, C2-6 alkanoyl; R2 = H, Me; R1, OR2 = isopropylidenedioxy; R3 = F, Cl, Br; R4 = H, Cl, F; R5 = H, F, Cl, Br; Z = O, H, OH, H, Cl) and their 1,2-didehydro derivs. Were prepared Thus, flumethasone was acetylated and then underwent enolization-methylation to give the methoxypregnatrienone II, which was fluorinated by FClO3, hydrolyzed, and then oxidized by O in MeOH containing K2CO3 to give androstadienecarboxylic acid III (R6 = HO; R7 = H). The latter was acylated by (EtCO)2O and then successively treated with (EtO)2F(O)Cl and MeSNa to give III (R6 = SMe; R7 = COBt) (IV). IV had antinflammatory activity 0.15 times that of fluocinolone but with little thymolytic activity.

REL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and enolization-methylation of)

RN 73205-13-7 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-methyl ester, (6a,118,16a,17a)- (CA INDEX NAME)

Absolute stereochemistry.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)

L41 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:252506 CAPLUS

DOCUMENT NUMBER: 148:308571

TITLE: Preparation of uronic acid derivatives as

metalloproteinase inhibitors

INVENTOR(S): Sattigeri, Viswajanani J.; Palle, Venkata P.; Khera,
Manoj Kumar; Reddy, Ranadheer; Tiwari, Manoj Kumar;

Soni, Ajay; Abdul Rauf, Abdul Rehman; Joseph, Sony; Musib, Arpita; Dastidar, Sunanda G.; Srivastava, Punit

Kumar

PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India

SOURCE: PCT Int. Appl., 183 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

FAMILY ACC. NUM. COUNT PATENT INFORMATION:

											LICAT						
WO	2008	0233	36		A2		2008	0228			2007-						
MO	2008																
	W:										, BG,						
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											, SL,			SY,	TJ,	TM,	TN,
											, ZA,						
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											, PT,						
											, ML,						
											, SZ,		UG,	ZM,	ZW,	ΑM,	ΑZ,
		BY,	KG,	ΚZ,	MD,	RU,	TJ,	TM,	ΑP,	EΑ	, EP,	OA					
					A1		2008	0228		AU :	2007-	2872	30		2		
	2661										2007-					0070	
EP											2007-						
	R:										, ES,						
							LV,	MC,	MΤ,	NL	, PL,	PT,	RO,	SE,	SI,	SK,	TR,
			BA,														
	2010										2009-						
MX	2009	0019	63		A		2009	0330		MX :	2009-	1963			2	0090	220
IN	2009	DN01	499		A		2009	0619		IN:	2009-	DN 14	99		2	0090	304
NO	2009	0011	69		A		2009				2009-						
	2009		22		A						2009-						
	1015		1		A		2009	0909			2007-						
							2010	0401		US :	2009-	4381	82			0091	
ORITY	Y APP	LN.	INFO	.:							2006-1						
											2007-					0070	821
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ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMA
OTHER SOURCE(S): CASREACT 148:308571; MARPAT 148:308571
GI

AB The present invention relates to β -hydroxy and amino substituted carboxylic acids I, wherein n is an integer from 1 to 5; R1 is H, optionally substituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, aralkyl, alkoxy, aryloxy, alkenyl-oxy or alkynyl-oxy; R2 is heterocyclyl, heteroaryl, NR4R5, -NHC(=Y)R4, -NHC(=Y)NR5Rx, -NHC(O)OR4, -NHSO4R C(=Y)NR4R5, C(O)OR6, wherein: Y is O or S, OR5, -OC(O)NR4R5, O-acyl, S(O)mR4, -SO2N(R4)2, cyanoamidino or quanidine; Rx is R4 or -SON(R4)2; R6 is H, alkyl, cycloalkyl, aralkyl, heteroarvl-alkvl, heterocyclyl-alkvl or cycloalkyl-alkyl, wherein: R4 is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, aralkyl, heteroaryl-alkyl, heterocyclyl-alkyl or cycloalkyl-alkyl; and m is an integer 0-2; R5 is H or R4; R3 is H, fluorine, alkyl, cycloalkyl-alkyl or aralkyl; A is OH, OR4, -OC(O)NR4R5, O-acyl, NH, NR4R5, -NHC(=Y)R4, -NHC(=Y)NR5Rx, -NHC(O)OR4, -NHSO2R4; Q is optionally substituted aryl or heteroaryl, which act as matrix metalloprotease inhibitors, particularly diastereomerically pure β-hydroxy carboxylic acids, corresponding processes for the synthesis of and pharmaceutical compns. containing the compds. of the present invention. Compds. of the present invention are useful in the treatment of various inflammatory, autoimmune and allergic diseases, such as methods of treating asthma, rheumatoid arthritis, COPD, rhinitis, osteoarthritis, psoriatic arthritis, psoriasis, pulmonary fibrosis, wound healing disorders, pulmonary inflammation, acute respiratory distress syndrome, perodontitis, multiple sclerosis, gingivitis, atherosclerosis, neointimal proliferation, which leads to restenosis and ischemic heart failure, stroke, renal diseases, tumor metastasis, and other inflammatory disorders characterized by the over-expression and over- activation of a matrix metalloproteinase using the compds. Thus, (2S,3R)-3-hvdroxy-2-[2-(4-oxo-1,2,3-benzotriazin-3(4H)v1)ethv1]-5-(4-pyrimidin-5-v1-phenv1)pentanoic acid was prepared and tested in rats as metalloproteinase inhibitor. Pharmacokinetic screening assays for Matrix Metallo Proteinase (MMP 9/12) inhibitors, are reported. Compds. of the present invention can be selective over MMP-1 by > 100 fold.

IT 8755-66-9, Cloticasone 90566-53-3, Fluticasone RL: BSU (Biological study, unclassified); BIOL (Biological study) (preparation of uronic acid derivs. as metalloproteinase inhibitors) RN 87556-66-9 CAPLUS

RN 8/556-66-9 CAPLUS CN Androsta-1, 4-diene-17-carbothioic acid, 6, 9-difluoro-11,17-dihydroxy-16-methyl-3-oxo-, S-(chloromethyl) ester, (6a.1B,16a.17-a) (CA INDEX NAME)

Absolute stereochemistry.

RN 90566-53-3 CAPLUS
Androsta-1,4-diene-17-carbothioic acid,
6,9-difluoro-11,17-dihydroxy-16-methyl-3-oxo-, S-(fluoromethyl) ester,
(6\alpha,11\beta,1\alpha,1\alpha,17\alpha) (CA INDEX NAME)

Absolute stereochemistry.

IT 25952-53-8, EDCI
 RI: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of uronic acid derivs. as metalloproteinase inhibitors)

RN 25952-53-8 CAPLUS

CN 1,3-Propanediamine, N3-(ethylcarbonimidoyl)-N1,N1-dimethyl-, hydrochloride (1:1) (CA INDEX NAME)

 $Et-N = C = N-(CH_2)_3-NMe_2$

● HC1

L41 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:857616 CAPLUS

DOCUMENT NUMBER: 141:332364

TITLE: Process for the preparation of steroidal carbothioic

acid derivatives and intermediates

INVENTOR(S): Loevli, Trond; Nygaard, Anne-mette; Reitstoen, Bjoern;

Fivelstad, Magny PATENT ASSIGNEE(S): Alpharma Aps. Den.

SOURCE: PCT Int. Appl., 40 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

	FENT																	
	2004																	
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,	
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		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NA,	ΝI,	
		NO,	ΝZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	
		ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW	
	RW:	BW,	GH,	GM,	KΕ,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	
							TJ,											
							HU,											
				BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	
		TD,																
EP	1466																	
	R:						ES,										PT,	
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	2004									AU 2	004-	2263	18		2	0040	402	
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										WU Z	004-	DICZ4	~		v: 2	0040	402	

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT CASREACT 141:332364; MARPAT 141:332364 OTHER SOURCE(S):

17β-carboxylic acid, prepared from flumetasone, in DMA was treated with EDC (1-ethyl-3-(3-dimethylaminopropyl)carbodimide) and NHS

(N-hydroxysuccinimide) followed by sodium hydrosulfide hydrate and then bromofluoromethane to give 92% S-fluoromethyl

6α,9α-difluoro-11β-hydroxy-16α-methy1-3-oxo-

AB Steroidal carboxthioc acids were prepared by reacting steroidal carboxylic acids or salts with a coupling agent alone or in conjunction with a coupling enhancer followed by reaction with a nucleophilic agent comprising a sulfur atom. Thus, 6α , 9α -difluoro- 11β -hydroxy- 16α -methyl-3-oxo- 17α -propionyloxyandrosta-1,, 4-diene-

 $17\alpha\text{-propionyloxyandrosta-1,4-diene-17}\beta\text{-carbothioate}$ (fluticasone propionate).

IT 73205-13-7P 80474-14-2P, Fluticasone propionate

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for preparation of steroidal carbothioic acid derivs. and intermediates)

RN 73205-13-7 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid,

6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-methyl ester, (6 α ,11 β ,16 α ,17 α)- (CA INDEX NAME)

Absolute stereochemistry.

RN 80474-14-2 CAPLUS

N Androsta-1, 4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, (6α,11β,16α,17α)- (CA INDEX NAME)

Absolute stereochemistry.

RN 80474-45-9 CAPLUS

CN Androsta-1, 4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, (6a,11B,16a,17a)- (CA INDEX NAME) Absolute stereochemistry. Rotation (-).

IT 25952-53-8, Edc

RL: RGT (Reagent); RACT (Reactant or reagent) (process for preparation of steroidal carbothioic acid derivs. and intermediates)

RN 25952-53-8 CAPLUS

CN 1,3-Propanediamine, N3-(ethylcarbonimidoy1)-N1,N1-dimethyl-, hydrochloride (1:1) (CA INDEX NAME)

Et-N=C=N-(CH2)3-NMe2

HC1

REFERENCE COUNT:

14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:837305 CAPLUS

DOCUMENT NUMBER: 141:332363

TITLE: Process for the preparation of steroidal

17β-carbothioates

INVENTOR(S): Loevli, Trond; Nygard, Anne Mette; Reitstoen, Bjoern; Fivelstad, Magny

PATENT ASSIGNEE(S): Alpharma Aps, Den.

SOURCE: Eur. Pat. Appl., 18 pp.

CODEN: EPXXDW
DOCUMENT TYPE: Patent

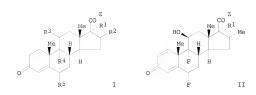
DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION:

	PATENT NO. EP 1466920																	
	1466	920			A1		2004	1013		EP 2	003-	7756			2	0030	404	
	R:						ES,										PT,	
							RO,											
	2004									AU 2	004-	2263	18		2	0040	402	
	2004		18		B2		2008	0605										
	2530				A1		2004	1014		CA 2	004-	2530	680		2	0040	402	
WO	2004																	
	W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	ΒY,	ΒZ,	CA,	CH,	
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,	
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	
		TJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW	
	RW:	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM.	AZ,	
		BY,	KG,	KZ,	MD,	RU.	TJ,	TM.	AT,	BE.	BG,	CH,	CY,	CZ,	DE.	DK,	EE,	
		ES.	FI.	FR.	GB,	GR.	HU.	IE.	IT.	LU.	MC.	NL.	PL,	PT.	RO.	SE,	SI,	
		SK.	TR.	BF.	BJ.	CF.	CG,	CI.	CM.	GA.	GN.	GO.	GW.	ML.	MR.	NE.	SN.	
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EP	1611				A1		2006	0104		EP 2	004-	7253	01		2	0040	402	
	R:	AT.	BE.	CH,			ES,											
							RO,											HI
CN	1798																	
JP	2006 2005	5220	28		т		2006	0928		JP 2	006-	5043	47		2	0040	402	
NO	2005	0046	36		A		2005	1227		NO 2	005-	4636			2	0051	010	
TN	2005	CN02	890		A		2007	0406		TN 2	005-	CN28	90		2	0051	103	
US	2007	0270	584		A1		2007	1122		US 2	007-	5521	18		2	0070	413	
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																0010	102	

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 141:332363 GI



- AB A novel method was disclosed for the conversion of steroidal 17β -carboxylic acids I (Z = OH) to the corresponding carbothioates I [R1 = H, OH, acyloxy; R2 = H, α -OH, α -, β -alkyl; R1R2 = fused 1,3-dioxolane ring of the form -OCR7R8O-; R3 = OH, protected hydroxyl; R4 = H, halogen; R3R4 = bond, -O- (epoxide); R5 = H, halogen; R7, R8 = H, alkyl; Z = SCH2F, SCH2Br, S(CH2)2F] including fluticasone propionate II (R1 = COCH2Me, Z = SCH2F), via novel in situ generated 17β -carboxy imidazolyl- or succinimidyl esters. Thus, flumetasone II (R1 = OH, Z = CH2OH) was oxidized using periodic acid to form the corresponding acid II (R1 = Z = OH) in 98% yield. The the acid was esterified with MeCH2COCl using NEt3 to give 17α -propionate II (R1 = OCOCH2Me, Z = OH) in 99% yield, and subsequent treatment of the 17α -propionate with NHS and FCH2Br gave fluticasone propionate in 75% yield.
- IT 25952-53-8, EDC

RL: RGT (Reagent); RACT (Reactant or reagent)

(process for the preparation of steroidal 17-carbothioates)
RN 25952-53-8 CAPLUS

CN 1,3-Propanediamine, N3-(ethylcarbonimidoyl)-N1,N1-dimethyl-, hydrochloride (1:1) (CA INDEX NAME)

Et-N=C=N-(CH2)3-NMe2

● HCl

IT 73205-13-7P 80474-14-2P, Fluticasone propionate 80474-45-9P RI: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for the preparation of steroidal 17β-carbothioates)

RN 73205-13-7 CAPLUS

N Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-methyl ester. (6a.118,16a.17a) - (CA INDEX NAME)

Absolute stereochemistry.

RN 80474-14-2 CAPLUS

CN Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester, (6a,11β,16a,17a)- (CA INDEX NAME)

Absolute stereochemistry.

RN 80474-45-9 CAPLUS

CN Androsta-1,4-diene-17-carbothioic acid,
6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-,
(6a,11B,16a,17a)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

3

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT